



Kidney in Cardiovascular Disease

Council Newsletter

Spring 2002

AMERICAN HEART ASSOCIATION KIDNEY IN CARDIOVASCULAR DISEASE

NEWSLETTER MISSION STATEMENT

The Kidney in Cardiovascular Disease Newsletter mission is as follows:

1. To promote communication and unity of purpose among the varied members of the Council on the Kidney in Cardiovascular Disease,
2. To promote communication between the Leadership Committee and Council members,
3. To disseminate information regarding research and educational activities, and
4. To promote initiatives for improved funding of research, education, and patient care.

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CHAIR

From the



It hardly seems possible that 19 months have passed since I assumed the Chairmanship of the Council on the Kidney in

Cardiovascular Disease of the American Heart Association. It has been a rewarding and exhilarating experience. Foremost among the pleasures has been the opportunity to get to meet and interact with so many of you. It is clear that the major reason that the Kidney Council has survived and grown is directly related to the dedication and activities of its membership. Thanks for making this such a memorable experience for me!

Several important events have occurred and a number of plans are in the offing. I am delighted that Dr. Tom Dubose will be taking over as your Chair. His vigor and ability to get things done augur well for the continued progress of our organization. Please accord him the kind and quality of support that you have provided to me.

Our membership continues to grow. This is a key issue, as you are aware. I thank the American Society of Nephrology and Dialysis Clinic, Inc., for their support in this venture. We have recently concluded discussions with the Council on High Blood Pressure Research to associate ourselves with them in a closer manner. This includes endorsing the journal *Hypertension* as the official journal of the Kidney Council, and developing a closer relationship with their annual meeting. At this time, we have arranged to be associated with them in the planning process with the ultimate goal to make this meeting an annual venture of BOTH Councils.

Finally, a group of Council members led by Dr. Anton Schoolwerth is engaged in the process of writing a Kidney Council "white paper" exploring the issue of kidney disease as a risk factor for the development of cardiovascular disease. We hope to utilize the advocacy of the American Heart Association to make this a major focus of the organization, as has been the case in the past for cholesterol, high blood pressure and stroke.

My thanks to all of you who have made my tenure as Chairman so enjoyable and worthwhile.

*Best regards,
Jules B. Puschett, MD*



Announcement:

56th Annual Fall Conference and Scientific Sessions of the Council for High Blood Pressure Research in association with the Council on the Kidney in Cardiovascular Disease

September 25-28, 2002
Disney's Contemporary Resort
Orlando, Florida

Information may be obtained through:

americanheart.org/conferences or
American Heart Association
Scientific Meetings
7272 Greenville Avenue
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email: scientificconferences@heart.org

Co-sponsored by the Council on Nutrition, Physical Activity, and Metabolism.

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EDITOR

Note from the



I thank Dr. John Scoble for his contribution to the Newsletter. His editorial highlights the important issue of atherosclerotic renal artery disease.

Dr. Anton Schoolwerth and colleagues have recently published an AHA Scientific Statement: Schoolwerth AC,

Sica DA, Ballerman BJ, Wilcox CS. Renal considerations in angiotensin converting enzyme inhibitor therapy. *Circulation* 116: 1985-1991 (2001). You can access it directly at the following URL: <http://circ.ahajournals.org/cgi/content/full/104/16/1985>

*Eric E. Simon, M.D.
Editor, Council on Kidney and
Cardiovascular Disease Newsletter*

PROGRAM

National Kidney Disease Education

The NIDDK has initiated a major project aimed at education of the general population (especially those at high risk) and health care providers about kidney disease along with promotion of its early detection. The National Kidney Disease Education Program (NKDEP) is directed by Thomas Hostetter, M.D. The goals of the program are to increase awareness of kidney disease along the lines of previous initiatives by the NIH such as the National Diabetes Education Program, the National High Blood Pressure Education Program, and the National Cholesterol Education Program. The NIDDK is investing significant resources in the hope that increased awareness and screening will impact the current epidemic of kidney disease. A Steering Committee comprising representatives of many organizations related to kidney disease,

hypertension, diabetes, minority health, etc., has met several times honing the goals and message. One tangible outcome will be a Web site (currently under construction) that will act as a clearinghouse for information about kidney disease, other kidney disease education programs and the status of the NKDEP initiative. The American Heart Association, Council on the Kidney, endorses these efforts, and I have been serving as the representative from the Kidney Council to the NKDEP. If any Kidney Council members have ideas, concerns, input, etc., about this program, please contact me.

Eric E. Simon, M.D.

*Member NKEPD Steering Committee for the
AHA Council on Kidney and Cardiovascular Disease*

REVIEW

Editorial

Atherosclerosis and the Kidney

*Dr. John E. Scoble, M.D., F.R.C.P.
Clinical Director Nephrology
Transplantation and Urology
Guys' and St. Thomas' Trust, London.*

It has been clear for many years that the overwhelming workload of the cardiologist is in the management of atherosclerotic cardiac disease. It has also been clear that for the vascular surgeon, all their practice will be involved in the management of atherosclerotic vascular disease. It does seem strange that the nephrologist whose organ lies between the vascular territories of the cardiologist and vascular surgeon has not recognized atherosclerotic renal disease as an important entity until recently⁽¹⁾. In fact, interest in renal artery disease has focused since the early work of Goldblatt on the Holy Grail of cure of hypertension⁽²⁾. The use of angioplasty in a non-atherosclerotic renal artery disease, such as fibromuscular dysplasia, has been extremely fruitful⁽³⁾. In this

condition, a 'cure' may be expected in the majority of patients presenting at a young age. However, the issue of intervention in atherosclerotic renovascular disease is less clear. Nephrologists might argue that coronary angioplasty has not been shown in a randomized trial to be better than medical therapy alone. In fact, in the only trial of medical therapy versus angioplasty, AVERT⁽⁴⁾, medical therapy was more effective than angioplasty! It has become clear that the relationship of atherosclerosis and the kidney is complex and interventions to improve outcome complex.

Although the issue of intervention in the majority of patients is unclear, it is fascinating that in the last fifteen years, a new syndrome has emerged after the

observations of Pickering, et al⁽⁵⁾. 'Flash Pulmonary Edema' is a clinical entity in which revascularization can cure the syndrome. A recent review of the published literature found the number of attacks of pulmonary edema before the diagnosis was made was approximately three⁽⁶⁾. In many instances, these attacks required ventilation! It now appears to be clear that in a group of patients with reasonable, although not usually perfect, left ventricular function, acute and unprovoked pulmonary edema occurs almost invariably at night. It may be that these patients have renal artery disease but maintain their nocturnal blood pressure fall resulting in a critical decrease in renal perfusion pressure. The subsequent literature has suggested that it is less common in patients with unilateral disease compared with

bilateral disease including occlusion on one side⁽⁷⁾. However, it does not appear to have been described in fibromuscular dysplasia. Most authorities would agree that this is an important indication for intervention in atherosclerotic renovascular disease with a frequently excellent clinical outcome^(5,7).

There has been significant discussion as to whether hypertension and atherosclerotic renal artery stenosis are linked in many cases. It could be that these are coexistent conditions in the same patient without a causal relationship between renal artery narrowing and hypertension. A large screening series of patients with coronary artery disease, which found that hypertension was not a predictive feature for the presence of renal artery narrowing, would seem to support this⁽⁸⁾. In fact, two small trials suggested that cure of hypertension in these patient was not seen with angioplasty for atherosclerotic renal artery stenosis^(9,10). The DRASTIC trial⁽¹¹⁾ supported this contention that angioplasty did not cure hypertension in these patients. It is important to point out that although the intervention group had angioplasty, in fact, half of the non-intervention group had angioplasty at the end of the year-long follow-up. It would appear clear that angioplasty has no place to play in the management of hypertension in patients with atherosclerotic renal artery disease. Is this true? The first comment is that the DRASTIC study only used angioplasty, whereas, subsequent studies have suggested that angioplasty plus stent insertion has better renal artery patency results⁽¹²⁾. However, at present there are no studies to suggest that this is mirrored in any improved functional outcome. A more subtle approach is to consider the management of these patients. Many authors, including this one, are hesitant to use angiotensin converting enzyme inhibitors (ACEI) or angiotensin II receptor blockers (ARB) in patients with severe bilateral renovascular disease. In spite of the excellent outcome of these agents in heart failure, hypertension, and progressive renal disease, these trials

have usually excluded patients with severe disease. The combination of ACEI, diuretic and acute volume depletion may lead to significant problems⁽¹³⁾. In some patients there is a severe worsening of renal function with the introduction of the agents. In this situation angioplasty can be considered as a method of smoothly instituting these agents with a positive outcome in improving risk-benefit for the individual patient⁽¹⁴⁾.

The role of atherosclerotic renal artery stenosis in renal dysfunction is less clear. The results from large studies have suggested that a considerable number of patients with end stage renal failure (ESRF) over the age of 60 years may have atherosclerosis as the cause of renal dysfunction^(15,16). In many ways this frequency reflects the pattern in cardiac disease in patients over the age of 60 years. However, it has been more difficult to ascertain the role of renal artery narrowing in atherosclerotic disease. Renal dysfunction and dialysis is a very rare complication of fibromuscular dysplasia. This suggests that renal artery narrowing alone is not the sole cause of renal dysfunction in atherosclerotic renovascular disease.

Early results by Harden, et al⁽¹⁷⁾ suggested that in patients with severe renovascular disease and significant renal dysfunction, intervention may have a positive role in altering the progression of renal dysfunction. This has been supported by a subsequent study showing a change in the rate of loss of renal function in similar patients⁽¹⁸⁾. However, a subsequent report has shown that even with successful angioplasty, progressive renal dysfunction can occur⁽¹⁹⁾. This report identified patients with effectively single functioning kidneys who had progressive renal dysfunction even after successful angioplasty. Angiography in these patients did not demonstrate restenosis as the cause of the progressive dysfunction.

There have been no randomized trials published to-date. Recent studies have shown that in atherosclerotic renal artery

stenosis, the presence of stenosis in unilateral disease does not predict the function in that kidney⁽²⁰⁾. This is illustrated by the observation that in individual patients with atherosclerotic disease, it was entirely random which kidney had worse function in unilateral disease⁽²⁰⁾. This is a very different pattern, than that seen with fibromuscular dysplasia which can be considered as a disease solely causing renal artery narrowing. This is supported by a number of publications that suggest that parenchymal disease in atherosclerotic nephropathy is not uniquely determined by renal artery narrowing⁽²¹⁾. It is clear that the presence of a severely atherosclerotic aorta above the renal arteries leads to renal dysfunction. Figure 1 shows the moieties present in an atherosclerotic plaque. These may have an effect on the kidney which lies immediately downstream from the plaque. The exact role of any of these substances is unclear but the evidence that the plaque can affect downstream function is shown by the biological marker of the cholesterol emboli. It is clear from the early postmortem studies that in the kidney of patients with severe atherosclerotic aortic disease cholesterol clefts could be found in many patients⁽²²⁾.

Atherosclerotic nephropathy is a term which embraces all these mechanisms of damage and differentiates the renal disease in this condition from any renal damage seen in conditions such as fibromuscular dysplasia.

The most important issue is to evaluate those patients who might benefit in terms of progressive renal dysfunction from intervention which is now almost entirely by renal angioplasty. Radermacher, et al⁽²³⁾ have shown that the resistive index can be a potentially powerful tool to predict those who will benefit from intervention. This study in unilateral disease analyzed the resistive index in the kidney contralateral to the stenosis. If the resistive index was high in the non-affected kidney then intervention was less successful. It is important to point out that the resistive index in the kidney with renal artery

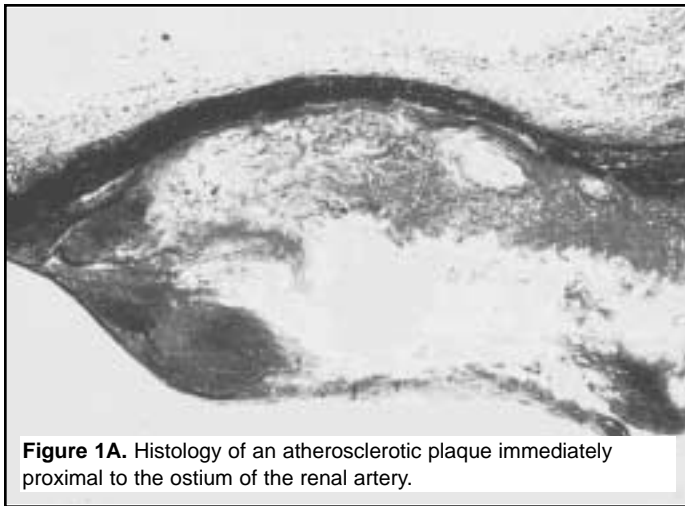


Figure 1A. Histology of an atherosclerotic plaque immediately proximal to the ostium of the renal artery.

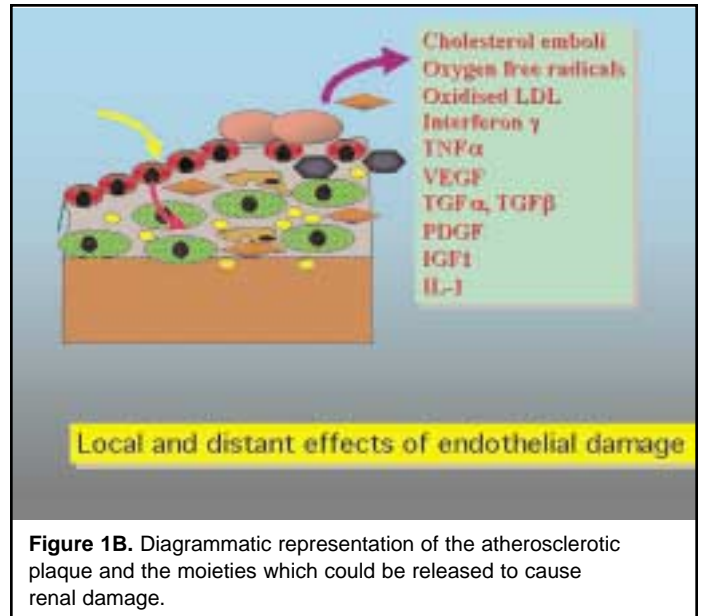


Figure 1B. Diagrammatic representation of the atherosclerotic plaque and the moieties which could be released to cause renal damage.

stenosis cannot be used as this will be low prior to angioplasty and rise after re-provision of adequate blood supply. However, even the authors of this study accept that intervention for patients approaching dialysis with tight stenosis in a single functioning kidney should be attempted (Dr. Radermacher personal communication).

The situation for the nephrologist is as complicated as that for the cardiologist with coronary artery narrowing except that renal artery narrowing is asymptomatic. The progression to ESRF is more complex in atherosclerotic disease than in other forms of renal artery narrowing. The management of atherosclerotic nephropathy may mirror that in coronary artery disease with a combination of medical therapy and intervention providing the best result. At present the STAR and ASTRAL randomized trials in Europe are attempting to address this issue.

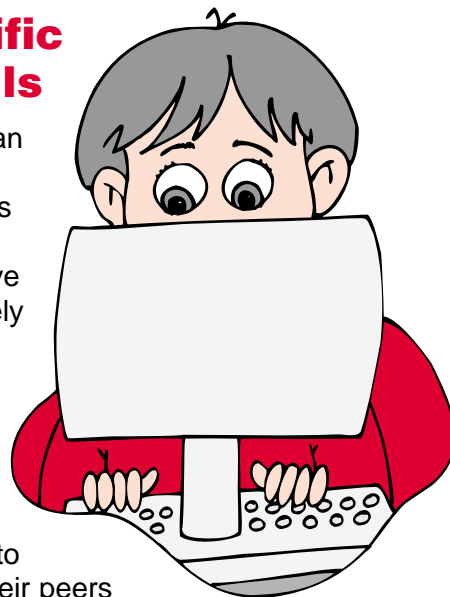
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Scientific Councils

The American Heart Association's 13 scientific councils have approximately 31,000 volunteer members and offer professionals an opportunity to work with their peers and preeminent researchers. Visit the Scientific Councils Web site at www.americanheart.org/councils/ for information about awards, scholarships, membership benefits, fellowship, council membership, Membership Directory, and Council newsletters.

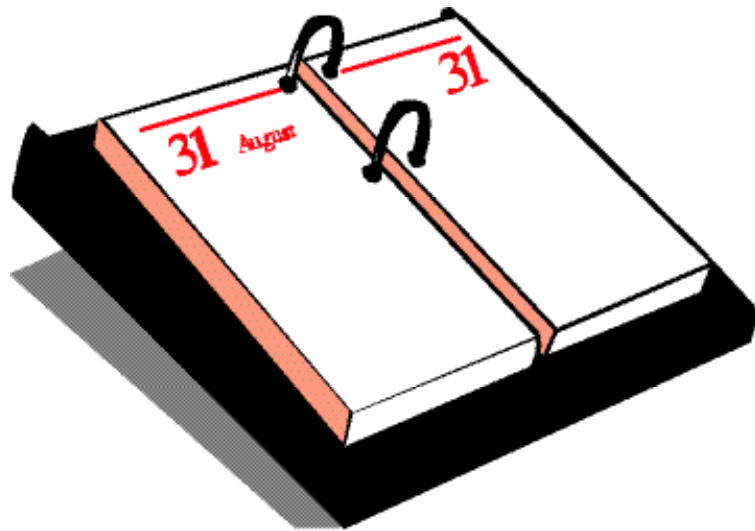


Fourth Hypertension Summer School

The CHBPR and the Council for the Kidney in Cardiovascular Diseases are co-sponsoring the Fourth Hypertension Summer School. This will be held from July 20–25, 2002. It will be in the historic campus of William and Mary College in Williamsburg, Virginia. The conference registration fees will be as low as possible. We hope that they will be in the range \$600–\$800, or possibly higher, depending on accommodations selected. The scope of this summer school will be expanded to include programs of interest to fellows and postdoctoral scientists in nephrology training programs. The subjects are designed to appeal to M.D. and Ph.D. graduates who wish to pursue careers in basic or clinical hypertension and related areas of nephrology, as well as to more experienced researchers, both basic and clinical, who need a refresher course that includes state-of-the-art reviews of new concepts and methods used in hypertension research. In the past, several M.D.s not actively involved in research have also attended and rated the summer school as a most valuable experience. Watch your mail for the conference brochure and the conference Web site: www.americanheart.org/conferences for more detailed information. Additional information and conference application forms will be available at this site.

CALENDAR

of Upcoming Events



Upcoming conferences that should be of interest to members of the Council are shown below. Meetings sponsored by the AHA and various AHA Councils and those sponsored by other societies are included.

April 27–28, 2002

Prevention VII: Obesity, A Worldwide Epidemic Related to Heart Disease and Stroke

Sponsored by the Councils on Nutrition, Physical Activity, and Metabolism; Epidemiology and Prevention; Cardiovascular Disease in the Young; Cardiovascular Nursing; Arteriosclerosis, Thrombosis and Vascular Biology; and Clinical Cardiology
Co-sponsoring organizations: NAASO, NIDDK, IASO, CDC
Hilton Hawaii Village, Honolulu, Hawaii

May 9–14, 2002

6-Day Symposium on Congenital Heart Disease Embryology, Pathology, Imaging and Surgery

Sponsored by the Councils on Cardiovascular Disease in the Young; Clinical Cardiology; Cardiovascular Radiology; and Cardio-Thoracic and Vascular Surgery
Hyatt Regency Albuquerque, Albuquerque, NM

July 20–24, 2002

4th AHA Hypertension Summer School

Sponsored by the Councils for High Blood Pressure Research and Kidney in CV Disease
College of William & Mary, Williamsburg VA

July 21–August 3, 2002

28th Ten Day Seminar on Epidemiology and Prevention of Cardiovascular Disease

Sponsored by the Council on Epidemiology and Prevention
Tahoe City, CA

August 21–25, 2002

Advances in the Molecular and Cellular Mechanisms of Heart Failure

Sponsored by the Council on Basic Cardiovascular Science
Co-sponsoring organizations: The Univ. of Maryland's Div. of Cardiology, Dept. of Med., Maryland Center for Heart, Hypertension and Kidney Disease, and the Dept. of Physiology; and the NIH/NHLBI
Snowbird Resort and Conference Center, Snowbird, UT

September 4–8, 2002

Grover Conference on Proinflammatory Signaling Mechanisms in the Pulmonary Circulation

Sponsored by the Councils of Cardiopulmonary & Critical Care; Basic Cardiovascular Science; Arteriosclerosis, Thrombosis and Vascular Biology; and Cardio-Thoracic and Vascular Surgery
Co-sponsoring organizations: PCF, ATS, APS
Lost Valley Ranch and Conference Center, Sedalia, CO (to be confirmed)

September 25–28, 2002

56th Annual Fall Conference & Scientific Sessions of the Council for High Blood Pressure Research and in association with the Council on Kidney in Cardiovascular Disease

Sponsored by the Councils for High Blood Pressure Research; Kidney in CV Disease; and Nutrition, Physical Activity, and Metabolism
Walt Disney World Contemporary Resort, Orlando, FL

October 12, 2002

Workshop, separate registration required.

October 13–14, 2002

4th Scientific Forum on Quality of Care and Outcomes Research in CVD and Stroke

Sponsored by AHA, ACC and the Dept. of Veterans Affairs
Omni Shoreham, Washington, DC

November 17–20, 2002

Scientific Sessions 2002

Chicago, IL
For further information:
Tel. 214-707-1543
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E-mail. sessions@heart.org

The American Heart Association would like to introduce it's newest line of digital products, the Heart Profilers™

The Heart Profilers are online, interactive tools designed to help patients and healthcare professionals understand treatment options and outcomes for specific cardiovascular disease states. Currently, information on coronary heart disease and congestive heart failure are available.

The Professional Heart Profiler is a patent-pending search engine for scientific publications. Its search technology is based on a Virtual Case Modeling (VCM) system which provides more intuitive and meaningful information than key word searches alone. The VCM system offers a unique interactive, "3D view" into scientific publications for unparalleled understanding of the science within a study. Healthcare Professionals can use this product to perform case modeling for a group of patients or to review recommended treatment for an individual patient. Patients can use this product to gain a greater understanding of their disease and the treatment options available to them.

Log on to the Heart Profilers at www.americanheart.org/heartprofilers

Have you heard of Get With The GuidelinesSM?

It's the American Heart Association's continuous quality improvement program for prevention of cardiovascular events and stroke.

*Get With The Guidelines*SM is a new guidelines-based hospital program that will help reduce deaths and the risk of recurrent heart attacks and strokes in patients with coronary and other vascular diseases. The *Get With The Guidelines* program provides tools and resources to assist medical professionals in building hospital systems to translate what we know about vascular disease secondary prevention into what is done in clinical practice. There will be several modules of the *Get With The Guidelines* program. Currently we are implementing the Coronary Artery Disease (CAD) module on a national basis. The Stroke module is in the pilot stage with an anticipated national launch in the fall of 2002.

Why is this an important program to the American Heart Association?

Studies have demonstrated significant improvement among patients when secondary prevention interventions are implemented while the patient is still in the hospital. Projections indicate that if the *Get With The Guidelines*

program is implemented nationwide, as many as 80,000 lives could be saved each year! The *Get With The Guidelines* program will also assist hospitals in complying with accreditation requirements for the Joint Commission on Accreditation of Healthcare Organizations (JCAHO); the performance measures of the Center for Medicare and Medical Services (formerly HCFA), and help managed care organizations comply with the National Committee for Quality Assurance (NCQA) HEDIS measures.

How does it work?

The *Get With The Guidelines* program works by mobilizing teams in acute-care hospitals to implement the American Heart Association's secondary prevention guidelines for patients with coronary and other vascular diseases. The program advocates using quality-improvement measures such as care maps, discharge protocols, standing orders and the online interactive patient management tool; all of which are based on the ACC/AHA secondary prevention guidelines.

For more information on this program visit our web site at www.americanheart.org/getwiththeguideines or send us an e-mail at guidelinesinfo@heart.org

Membership Application



Fighting Heart Disease and Stroke

We Want YOU To Join A Scientific Council

Each of the American Heart Association (AHA) 13 Scientific Councils represent a specialty dedicated to achieving the association's goals. More than 32,000 members participate in committees that determine how our research funding is allocated, which programs and abstracts will be presented at our Scientific Sessions and other AHA scientific conferences and participate in writing groups that produce scientific statements and guidelines. In addition, Scientific Council members receive the following benefits:

- **Early registration and reduced registration fees to AHA's annual Scientific Sessions and other council-sponsored meetings**
- **Discount!** Reduced subscription fees to AHA Scientific Journals including Arteriosclerosis, Thrombosis, and Vascular Biology; Circulation; Circulation Research; Hypertension; and Stroke
- Newsletters with updates on council activities and issues of interest to members
- On-line access to membership directory, expertise directory, and council home pages
- Opportunity to apply for council-sponsored scholarships and travel stipends
- Opportunity to meet and network with your peers

Join Online by visiting the AHA Web site at www.americanheart.org, and follow the links to Councils.

The 13 scientific councils are:

- Arteriosclerosis, Thrombosis, and Vascular Biology. \$45
Please select one or more sections in which you would like to be identified:
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- Basic Cardiovascular Sciences. \$40
 Trainees, graduate students and postdoctoral fellows. \$25
- Cardiopulmonary and Critical Care. \$35
 Nurses, trainees and allied health personnel. \$20
- Cardiovascular Disease in the Young \$50
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