

Hypertension

Editor's Comments

The American Society of Hypertension has passed the co-editorship of *Current Concepts in Hypertension* on to Dr. Joseph Izzo and myself. Our goal will be to build upon the quality and content that Drs. Frishman and Kaplan provided in earlier editions. We offer commentaries on three recent publications in this issue. One addresses the effects of comprehensive nutritional therapy on multiple cardiovascular risk factors, the second discusses the ongoing controversy surrounding pharmacologic therapy for high blood pressure, and the third reports a curious finding related to a long-standing absolute in nutrition and blood pressure. We appreciate the assistance of the authors in preparing these summaries for inclusion here.

For its first meeting outside of New York City, the American Society of Hypertension has chosen the marvelous city of San Francisco this year. The anticipated record attendance at the meeting reflects the continued growth of the ASH and its importance as a forum for advancing our understanding of how best to manage the patient with high blood pressure and prevent future generations from developing this disorder.

—David A. McCarron, MD

Nutritional Management of Cardiovascular Risk Factors

Dietary modifications are commonly recommended for the treatment of a variety of chronic medical conditions including hypertension, dyslipidemia, and non-insulin-dependent diabetes mellitus (NIDDM). However, adherence to dietary recommendations for disease management is often hindered by the complexity of incorporating them into the daily diet. Furthermore, while the effects of isolated changes in the diet on specific conditions have been well-documented, much less is known about the effects of implementing the myriad of dietary recommendations on multiple cardiovascular risk factors.

The Cardiovascular Risk Reduction Dietary Intervention Trial was designed to assess these effects in a 4-year series of studies initiated in 1995 by the Vanguard Study Group. The first study in the series examined the clinical effects of a nutritionally-complete prepackaged meal plan that incorporated all American Heart Association and National Academy of Sciences National Research Council recommended dietary allowances (RDAs) for vitamins, minerals, and macronutrients, compared with a patient-selected diet based on the ADA exchange list system. The study included a 4-week baseline period with a 10-week intervention and bi-weekly clinic visits.¹

Effects of Nutritional Management Mean Differences Between Baseline and Clinical Values

Measure	CCNW	Self-directed Diet Group	P
Systolic BP (mm Hg)	-6.4 ± 9.2	-4.6 ± 9.0	0.02
Diastolic BP (mm Hg)	-4.2 ± 5.7	-3.0 ± 5.1	0.006
Cholesterol (mg/dL)	-12.4 ± 22.5	-10.4 ± 21.9	0.30
Glucose (mg/dL)	-11.75 ± 34.0	-13.5 ± 36.6	0.10
HbA _{1c} (%)	-0.4 ± 0.8	-0.3 ± 0.7	0.56
Weight loss (kg)			
Male	-4.5 ± 3.6	-3.5 ± 3.3	
Female	-4.8 ± 3.0	-2.8 ± 2.8	

Table 1

Editorial Board

Co-Editors

Joseph Izzo, MD
State University of New York

David A. McCarron, MD
Oregon Health Sciences University

Managing Editor

William E. James, PhD
Postgraduate Institute for Medicine

Stevio Julius, MD, ScD
The University of Michigan Medical Center

Robert A. Kloner, MD, PhD
The Heart Institute
University of Southern California

Laurence R. Krakoff, MD
Mount Sinai School of Medicine
Englewood Hospital & Medical Center

Franz H. Messerli, MD, FACC, FACP
Ochsner Clinic

Michael A. Weber, MD
The Brookdale Hospital Medical Center

This multicenter, randomized, parallel-intervention trial was conducted at 10 medical centers in the United States and Canada and involved 560 men and women with hypertension, dyslipidemia, or NIDDM. During the 4-week baseline period, nutrition prescriptions were calculated for each participant to meet individual energy requirements based on the Harris-Benedict equation and adjusted for physical activity levels. Participants were then randomized to the Campbell's Center for Nutrition and Wellness (CCNW) plan, which includes prepackaged breakfast, lunch, and dinner meals provided to participants, or to a nutritionist-guided diet derived from exchange lists in which participants self-selected foods to meet their nutrition prescription for 10 weeks. Blood pressure (BP); lipid, glucose, glycosylated hemoglobin (HbA_{1c}), and insulin levels; body weight; dietary intake; and quality of life were measured repeatedly throughout the intervention.

The results of the study demonstrated improvements from both diet plans in BP, lipid levels, carbohydrate metabolism (Figs 1-3), weight, and quality of life ($P \leq .001$) for all findings except the low-density lipoprotein to high-density lipoprotein ratio ($P = .25$). Mean differences (\pm SD) between baseline and treatment clinical values for the CCNW and the self-selected diet groups (between-group P values), are shown in Table 1.

Quality of life significantly improved for daily and work activities ($P < .05$) and nutritional health perceptions ($P < .005$) with the CCNW plan relative to the self-selected group. Overall nutrient intake and compliance were both significantly better ($P < .001$) with the CCNW plan. This study demonstrated dietary programs that meet the recommendations of national health organizations improve multiple risk factors for cardiovascular disease, even in persons with high-normal risk profiles. Improvements in clinical endpoints, quality of life, compliance, and nutritional adequacy of the diet were greater with the CCNW plan than with the self-selected diet.

In a second study in this series we assessed the same endpoints using similar dietary interventions for 10 weeks but reduced the amount of contact with participants to the level that would occur in actual clinical practice when dietary therapy is recommended.² Results from this usual care approach were remarkably similar to the first study in this series. Further extending the "real world" application of the CCNW meal plan, the third study in this trial is currently underway. This 1-year study includes a total of 330 participants at university medical centers in New York, Alabama, California, Pennsylvania, and Oregon, and will determine the long-term acceptability and effectiveness of the comprehensive meal plan for cardiovascular risk reduction.

The results of the study demonstrated improvements from both diet plans in BP, lipid levels, carbohydrate metabolism, weight, and quality of life"

This study demonstrated dietary programs . . . improve multiple risk factors for cardiovascular disease, even in persons with high-normal risk profiles."

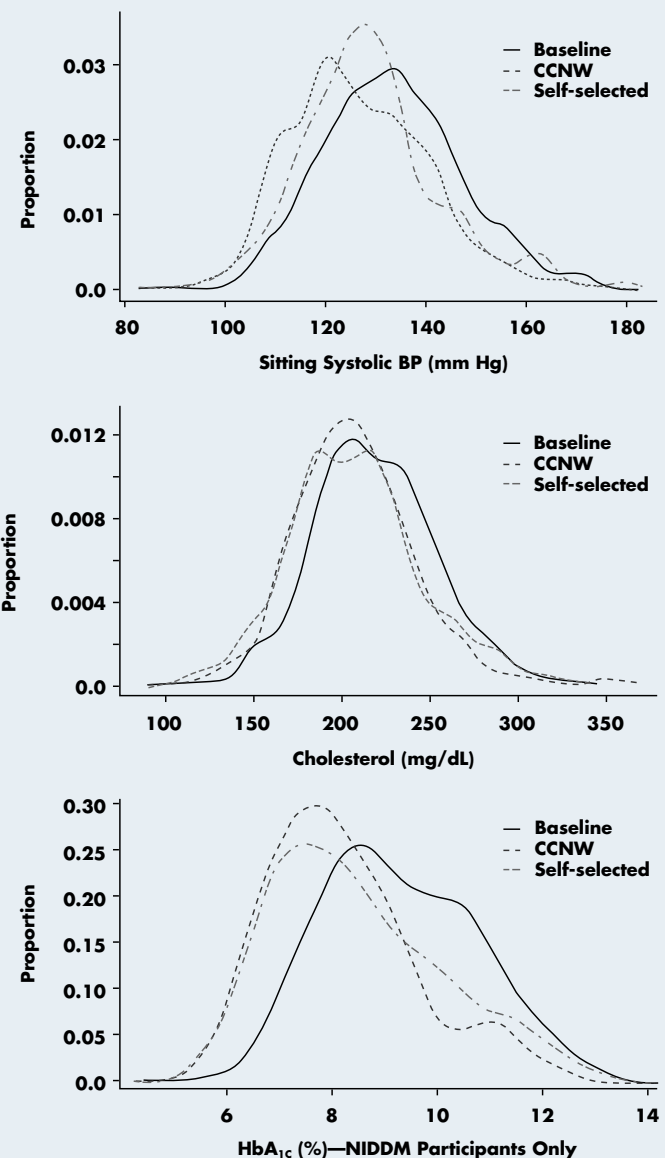
David A. McCarron, MD
 Professor of Medicine
 Oregon Health Sciences University
 Portland, Oregon

References

1. Arch Intern Med 1997; 157:169-177.
2. Hypertension 1996; 28:510 [abst. #10].

Distributions of Primary Endpoints at Baseline and With the Two Interventions¹

(Proportion signifies the fraction of the cohort)



Copyright © 1997, American Medical Association

Figures 1-3

Health Outcomes Associated With Antihypertensive Therapies Used as First-line Agents. A Systematic Review and Metaanalysis

Rationale. In 1993 the fifth Joint National Committee on the Detection, Evaluation, and Treatment of High Blood Pressure (JNC-V) limited its recommendation of first-choice therapy for hypertension to low-dose diuretics and β -blockers “unless they are contraindicated or unacceptable, or unless there are special indications for other agents.”¹ Utilizing MEDLINE searches and previous metaanalyses, we reviewed the scientific evidence underlying JNC-V recommendations to assess safety and efficacy of various antihypertensive therapies used as first-line agents and evaluated them in terms of major disease endpoints.²

Study selection. Long-term (at least 1-year) studies that assessed major disease endpoints as an outcome were chosen. For the metaanalysis, we selected placebo-controlled randomized trials. Clinical trials were classified according to the primary treatment strategy used in the active group. For randomized trials using surrogate endpoints such as blood pressure, we selected the largest studies that evaluated multiple drugs. Information from observational studies was used where clinical trial evidence was lacking.

Results. Diuretics and β -blocker therapy were evaluated in 18 long-term randomized trials. Compared with placebo, β -blocker therapy effectively prevented stroke (relative risk [RR], 0.71; 95% confidence interval [CI], 0.59 to 0.86) and congestive heart failure RR, 0.58; 95% CI, 0.40 to 0.84). The findings were similar for high-dose diuretic therapy (for stroke, RR, 0.49; 95% CI, 0.39 to 0.62; and for congestive heart failure, RR, 0.17; 95% CI, 0.07 to 0.41). Low-dose diuretic therapy prevented not only stroke (RR, 0.66; 95% CI, 0.55

to 0.78) and congestive heart failure (RR 0.58; 95% CI, 0.44 to 0.76) but also coronary disease (RR, 0.72; 95% CI, 0.61 to 0.85) and total mortality (RR, 0.90; 95% CI, 0.81 to 0.99).

Although calcium channel blockers and angiotensin-converting enzyme inhibitors reduce blood pressure in hypertensive patients, the clinical trial evidence for health outcomes is limited. The available evidence for several short-acting dihydropyridine calcium channel blockers suggests the possibility of harm. Whether the long-acting formulations and the nondihydropyridine calcium channel blockers are safe and prevent major cardiovascular events in patients with hypertension remains untested and, therefore, unknown.

Conclusion. Based on the available scientific evidence, our study provides strong support for the current JNC-V recommendations of diuretics and β -blockers as first-line agents and low-dose therapy for all antihypertensive medications.

Bruce M. Psaty, MD, PhD

Co-Director, Cardiovascular Health Research Unit

Departments of Medicine and Epidemiology and Health Services

University of Washington

Seattle, Washington

References

1. Arch Intern Med 1993; 153:154-183.
2. JAMA 1997; 277:739-745.

Metaanalysis of Randomized, Placebo-controlled Clinical Trials in Hypertension According to First-line Treatment Strategy

Outcome Drug Regimen	Dose	Number of Trials	Events, Active Treatment/Control	RR (95% CI)
Stroke				
Diuretics	High	9	88/232	0.49 (0.39-0.62)
Diuretics	Low	4	191/347	0.86 (0.55-0.78)
β -blockers	High	4	147/335	0.71 (0.59-0.86)
HDFP	High	1	102/158	0.64 (0.50-0.62)
Coronary Heart Disease				
Diuretics	High	11	211/331	0.99 (0.83-1.18)
Diuretics	Low	4	215/363	0.72 (0.61-0.85)
β -blockers	High	4	243/459	0.83 (0.80-1.09)
HDFP	High	1	171/189	0.90 (0.73-1.10)
Congestive Heart Failure				
Diuretics	High	9	8/35	0.17 (0.07-0.41)
Diuretics	Low	3	81/134	0.58 (0.44-0.76)
β -blockers	High	2	41/175	0.58 (0.40-0.84)
Total Mortality				
Diuretics	High	11	224/382	0.88 (0.75-1.03)
Diuretics	Low	4	514/713	0.90 (0.81-0.99)
β -blockers	High	4	383/700	0.95 (0.84-1.07)
HDFP	High	1	349/419	0.83 (0.72-0.95)
Cardiovascular Mortality				
Diuretics	High	11	124/230	0.78 (0.52-0.97)
Diuretics	Low	4	237/390	0.76 (0.65-0.89)
β -blockers	High	4	214/410	0.69 (0.76-1.05)
HDFP	High	1	195/240	0.81 (0.57-0.97)

Trials had at least one endpoint of interest. HDFP refers to the Hypertension Detection and Follow-up Program Study (5484 subjects in stepped care and 5455 in referred care). For these comparisons, the numbers of participants randomized to active therapy and placebo were 7768 and 12,075 for high-dose diuretic therapy; 4305 and 5116 for low-dose diuretic therapy; and 6738 and 12,147 for β -blocker therapy. Because the Medical Research Council trials included 2 active arms, the placebo group is included twice in these totals, once for a diuretic comparison and again for β -blocker comparison. The total number of participants randomized to active therapy and control therapy are 24,294 and 23,925 respectively.

Adapted from JAMA 1997; 277:739-745.

Table 1

Age, Migration, and Blood Pressure in the Panamanian Kuna

Genetic/environmental interactions are central to the pathogenesis of our most common ills, including essential hypertension. The remarkable complexity of the interaction between multiple genes and multiple external factors has limited progress, although these relationships can be explored effectively, as demonstrated by agricultural research, when expression of each genotype can be examined under multiple environmental conditions. Although in humans a similar study design is impossible, the migration experience provides a reasonable analogy.

In the case of migration and hypertension, recent reviews cite 39 indigenous populations with low blood pressure (BP) in Africa, the Americas, and the Pacific Region. Whenever the migration has occurred the protective factor has been shown to be primarily environmental, rather than genetic, because BP rose without exception following migration to an urban environment. Among the lines of evidence suggesting a role for salt intake as an environmental contributor to pathogenesis has been the identification of these isolated communities where salt intake is low, hypertension is rare, and BP does not rise with age. Indeed, by 1976, Lot Page concluded all low BP populations have a low salt intake as their major protective mechanism.

“... by 1976, Lot Page concluded all low BP populations have a low salt intake as their major protective mechanism.”

We recently extended migration studies to the Kuna Indians who have resided for centuries in the San Blas Island chain, an archipelago off the Caribbean coast of Panama.¹ A remarkably low level of mitochondrial gene diversity in the Kuna suggests they have experienced little genetic admixture and are the product of a population bottleneck. We confirmed the rarity of hypertension and absence of an age-related BP rise in island-dwelling Kuna and showed this population also had a BP pattern that reflected environmental linkages as BP rose with age. Hypertension prevalence was strikingly higher in Kuna who had moved to Panama City and its suburbs.

What is unusual in this population is that island-dwelling Kuna remain normotensive despite a high salt intake. Moreover, increased body weight is uncommon and does not parallel BP. Salt is added to food by the indigenous, island-dwelling Kuna so average intake is 210 ± 22 mEq per day based on 24-hour recall, as confirmed by a food frequency questionnaire and direct measurement of sodium content of 24-hour urine collections. The possible contribution of other nutrients such as potassium, magnesium, and fiber; a low protein intake; or some combinations requires further study.

“... island-dwelling Kuna remain normotensive despite a high salt intake.”

“... a low sodium intake is by no means universal as a protective mechanism in indigenous peoples.”

Alternatives to nutrition, such as stress, must also be considered. What is clear is that a low sodium intake is by no means universal as a protective mechanism in indigenous peoples. Because weight gain and increased salt intake have been universal in earlier studies, the partial acculturation in situ of island-

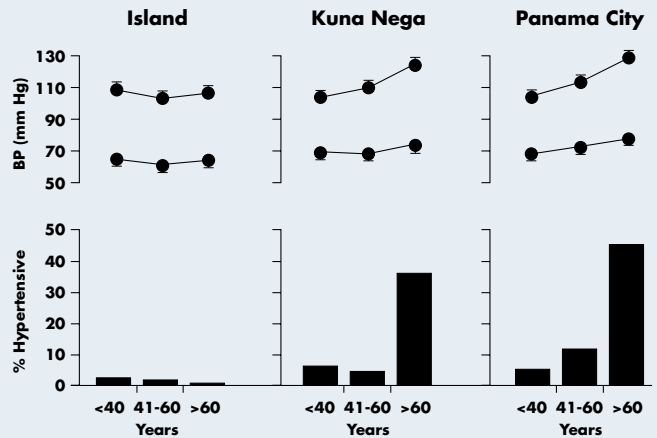
dwelling Kuna who are still protected provides an attractive situation for examining alternative mechanisms.

Norman K. Hollenberg, MD, PhD
 Professor of Medicine
 Harvard Medical School
 Boston, Massachusetts

Reference

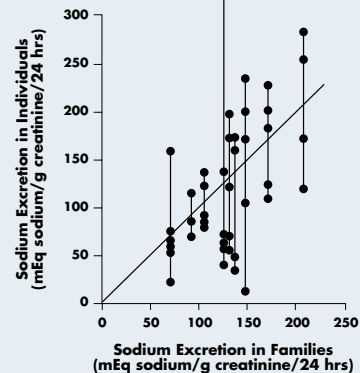
- Hypertension 1997; 29:171-176.

Relation Between Age, BP, and Hypertension Prevalence in Three Kuna Communities¹



Kuna Nega is a suburban community, inhabited only by Kuna Indians that allows them to maintain some, but not all, of their island lifestyle. Note that both systolic and diastolic BPs rise significantly with age in the Kuna residing in Kuna Nega and Panama City, but not on the isolated island ($P < .001$). Hypertension is much more prevalent in both communities than in the island dwellers.

Sodium Excretion in Families and Individuals¹



Relation between average excretion of sodium in 9 island-dwelling families (abscissa) versus the individual values in each family (ordinate). Salt intake and excretion were substantial in island-dwelling Kuna who are protected from hypertension and age-related rise in blood pressure. Only 5 of the 50 subjects showed a sodium excretion level similar to those reported for other isolated, normotensive cultures.

Please help us enhance the effectiveness of this publication.

You can help us evaluate and continue to improve this publication. Please take a minute to rate the following and return them to us.

Interest Level

- Angiotensin Antagonists and Renin Inhibitors High Medium Low
- Debating the Use of Diuretics High Medium Low
- How Low Should Blood Pressure Be? High Medium Low
- Hypertension in Minority Populations High Medium Low
- Treatment of Isolated Systolic Hypertension High Medium Low
- Individualized Hypertensive Workshops High Medium Low
- White-coat Hypertension High Medium Low
- Age and Gender Issues High Medium Low
- Safety of Long-acting Calcium Channel Blockers High Medium Low
- Dietary Fiber Supplementation and Blood Pressure High Medium Low
- Mean Office Versus Ambulatory Blood Pressure High Medium Low
- New Trends in Combination Therapy High Medium Low
- Pregnancy and Hypertension High Medium Low
- Renal Artery Disease in the Elderly High Medium Low
- Treating Hypertension in the Elderly High Medium Low
- Exercise and Hypertension High Medium Low
- Diet and Hypertension High Medium Low

Past Issues

- The content improves my professional effectiveness. High Medium Low
- The format is convenient and effective. High Medium Low
- The topics are clinically relevant. High Medium Low

Other suggested topics:

Thanks for your help!

Joseph Izzo, MD
 David A. McCarron, MD
 Co-Editors
Current Concepts in Hypertension

Fold Here, Tab or Tape, No Staples

PLACE
STAMP
HERE

American Society of Hypertension

The American Society of Hypertension (ASH) is the largest US organization dedicated exclusively to hypertension and related cardiovascular disease. ASH was founded in 1985 by Dr. John Laragh and 16 other world-famous clinicians and scientists in an effort to evaluate the vast accumulation of data on hypertension and to provide a separate forum for those involved in the study or management of high blood pressure. The mission of the Society became “to organize and conduct educational activities designed to promote and encourage the development, advancement, and exchange of scientific information in all aspects of research, diagnosis, and treatment of hypertension, and related cardiovascular diseases.”

Today, the Society boasts a membership of over 3,000 strong with 95% of its members holding an MD, PhD, or other advanced degree. The Society continues to fulfill its mission by annual meetings that provide registrants with the rare opportunity to exchange information and ideas with more than 2,500 fellow scientists from around the world. Highlights of the meeting include state-of-the-art lectures by renowned faculty, plenary sessions, original communications, poster presentations, technical and scientific exhibits, and provocative special symposia.

In addition, the Society publishes the prestigious *American Journal of Hypertension*, a monthly publication containing the latest information in both basic science and clinical research.

Membership in ASH is open to all those who have undertaken and accomplished meritorious original scientific investigation in the field of hypertension and/or related cardiovascular disease, those involved in the diagnosis and treatment of hypertension and related cardiovascular disease, and those with a demonstrated serious interest in the field. Among the benefits of ASH membership are association and interaction with clinicians and scientists who are world leaders in the field, a subscription to the *American Journal of Hypertension* and all its supplements, a listing in the ASH Member Directory used for patient referral, and a savings of 50% or more on registration fees for the annual scientific meeting.

The American Society of Hypertension sponsors three award programs annually. The first award program focuses on the area of ongoing research training in the field of hypertension for young clinicians planning a career in academic medicine. Another recognizes and rewards three scientists who have carried out a significant body of work in the field of hypertension or related cardiovascular diseases. The last award program recognizes and rewards five young physicians, currently residents or fellows, who have a demonstrated interest in the study of hypertension or who plan a career change into the field.

For further information on ASH membership, awards programs, future meeting dates or to add your name to the ASH mailing list, contact:

The American Society of Hypertension

515 Madison Avenue, Suite 1212

New York, NY 10022

Phone: 212-644-0650

Fax: 212-644-0658

Published by Postgraduate Institute for Medicine • Englewood, CO • 800-423-3576 • Copyright® 1997 • All rights reserved

 **The American Society of Hypertension**
515 Madison Avenue, Suite 1212 • New York, NY • 10022

NONPROFIT ORG. U.S. POSTAGE PAID PERMIT NO. 489 DENVER, CO
