Facts and principles learned at the 30th Annual Williamsburg Conference on Heart Disease

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The following represents our interpretation of the lectures presented at the 30th Annual Williamsburg Conference on Heart Disease, which was sponsored by the American College of Cardiology in cosponsorship with the Baylor Heart and Vascular Institute of Baylor University Medical Center and held December 7–11, 2002, in Williamsburg, Virginia. We have attempted to derive principles and to relay key, clinically useful facts.

ROLE OF THE ENDOTHELIAL CELL IN PREVENTING CORONARY HEART DISEASE

Robert A. Vogel, MD, Professor of Medicine and Director of Clinical Vascular Biology, Former Chief of the Division of Cardiology, University of Maryland School of Medicine, Baltimore, Maryland

1. Endothelial cell dysfunction, a reversible process, precedes atherosclerosis.
2. Hyperlipidemia, hypertension, cigarette smoking, obesity, inactivity, older age, and diabetes mellitus are various atherosclerotic risk factors that worsen endothelial cell function.
3. Lowering levels of blood lipids, blood pressure, blood glucose, and body weight, discontinuing cigarette smoking, exercising regularly, and drinking relatively small quantities (<30 g) of alcohol daily improve endothelial cell function.
4. Frequent laughter, a good marriage, owning and loving a dog, having few children, and having a satisfying occupation with adequate decision-making options are several nonatherosclerotic factors that also improve endothelial cell function.
5. Aging unaccompanied by regular exercise worsens endothelial cell function, but aging accompanied by regular exercise prevents the usual endothelial cell dysfunction of aging.
6. High-fat meals cause acute deterioration of endothelial cell function. A single typical fast-food meal causes transient endothelial cell dysfunction to an extent similar to that produced by smoking 2 cigarettes.
7. Endothelial cell dysfunction does not occur in individuals whose serum low-density lipoprotein (LDL) cholesterol is <80 mg/dL, whose peak systolic blood pressure is <120 mm Hg, whose body mass index is between 20 and 25 kg/m^2, who never smoke cigarettes, and who exercise regularly.
8. Alcohol (irrespective of beer, wine, or spirits) <30 g/day raises serum high-density lipoprotein (HDL) cholesterol, plasminogen, and tissue plasminogen activator and decreases serum lipoprotein (a), C-reactive protein (CRP), fibrinogen, and platelet aggregation.

USEFULNESS OF C-REACTIVE PROTEIN IN PREDICTING AND DIAGNOSING MYOCARDIAL ISCHEMIA AND IN EVALUATING ANTIISCHEMIC THERAPY

Eric J. Topol, MD, Provost and Chief Academic Officer, The Cleveland Clinic Foundation; Chairman, Department of Cardiovascular Medicine; Director, Joseph J. Jacobs Center of Thrombosis and Vascular Biology; Vice Chairman, Department of Molecular Cardiology; and Co-director, The Heart Center, Cleveland, Ohio

1. Topol considered high-sensitivity (hs)-CRP a more important predictor of coronary artery disease than an elevated LDL cholesterol level (odds ratio 4.5 vs 2.2).
2. Lowering serum total and LDL cholesterol, lowering blood pressure and body weight, discontinuing smoking, and taking some drugs (aspirin, clopidogrel, rosiglitazone) decrease CRP levels, and hypercholesterolemia, hypertension, obesity, cigarette smoking, and estrogen treatment increase CRP levels.
3. Topol suggested that measuring hs-CRP is not only useful as a predictor of coronary artery disease but may be useful in diagnosing myocardial ischemia and in following response to antiischemic therapy in coronary patients. Topol proposed that doing hs-CRP determinations in the emergency room may help separate patients with ischemic chest pain from those with nonischemic pain.
4. Whether lowering the hs-CRP will decrease atherosclerotic events is as yet undetermined.

INTRAVASCULAR ULTRASONIC ASSESSMENT OF ATHEROSCLEROSIS

Steven E. Nissen, MD, Vice Chairman, Department of Cardiology, Cleveland Clinic Foundation, Cleveland, Ohio

1. Coronary angiography shows only the lumen of the artery and provides relatively little information on the total quantity of atherosclerotic plaque present in the artery. The unit of measurement is diameter reduction.
2. Intravascular ultrasound (IVUS) imaging provides cross-sectional views of the artery and therefore displays both the amount of lumen and the amount of underlying plaque. The unit of measurement is cross-sectional area.

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3. IVUS imaging has demonstrated that the wall of the artery containing plaque expands outwardly such that the size of the lumen is not altered until a considerable quantity of plaque has actually been deposited in the lumen.
4. IVUS is very useful in studying reversibility of plaques. Statins and angiotensin-converting enzyme inhibitors have been shown to reduce plaque quantity.
5. By IVUS, 20% of Americans have coronary plaques by age 20.

EFFECTIVENESS OF ALDOSTERONE-RECEPTOR BLOCKADE AFTER MYOCARDIAL INFARCTION, IN SYSTEMIC HYPERTENSION, AND IN CONGESTIVE HEART FAILURE

Bertram Pitt, MD, Professor of Internal Medicine and Associate Chairman for Academic and Industrial Programs, Department of Internal Medicine, University of Michigan School of Medicine, Ann Arbor, Michigan

1. Blockade of the renin-angiotensin-aldosterone system using angiotensin receptor blockers improves endothelial cell function and reduces experimentally induced atherosclerosis. Aldosterone increases angiotensin I, which in turn increases angiotensin II, which inactivates nitric oxide, which probably increases atherosclerotic plaque formation. Elevation of aldosterone also increases free radicals, vascular inflammatory cells, myocardial mass, and collagen and vascular channels between myocardial fibers.
2. Angiotensin-converting enzyme inhibitors, even when used in conjunction with angiotensin receptor blockers, do not totally block aldosterone production. Aldosterone antagonists, such as spironolactone or eplerenone, provide additional blockage.
3. Aldosterone antagonists may prove to be beneficial in all patients who take angiotensin-converting enzyme inhibitors or angiotensin receptor blockers.

INTERVENTIONAL CARDIOLOGY—THE BATTLE AGAINST RESTENOSIS

Albert E. Raizner, MD, Professor of Medicine, Baylor College of Medicine; Director, Cardiac Catheterization Laboratory, Methodist Hospital; and Medical Director, Methodist DeBakey Heart Center, Houston, Texas

1. Although it is not useful in preventing restenosis at sites of balloon angioplasty, radiation (brachytherapy) has proven useful at sites of restenosis within previously implanted stents.
2. Restenosis occurs within noncoated stents about 30% of the time.
3. In contrast to noncoated stents, stents covered with certain immunosuppressive drugs (rapamycin, sirolimus, and paclitaxel) rarely (2% at 2 years) develop restenosis within the stents.

OPERATIVE STRATEGIES IN CORONARY AND VALVULAR HEART DISEASE

Charles S. Roberts, MD, Cardiothoracic Surgeon, Winchester Memorial Hospital, Winchester, Virginia

1. Compared with "off-pump" coronary bypass, Roberts prefers "on-pump" bypass because more conduits can be inserted and therefore a higher degree of revascularization can be achieved, with fewer acute conduit occlusions. "Off-pump" coronary bypass, however, yields shorter hospital stays and fewer bleeding complications.
2. The use of left internal mammary artery conduits in coronary artery bypass grafting is now considered the standard of care. The concurrent use of the right internal mammary artery, however, should be avoided in patients who are >65 years of age, have diabetes mellitus or chronic obstructive lung disease, or are obese because these patients have a higher rate of mediastinitis.
3. Coronary artery bypass grafting in patients with acute myocardial infarction should be delayed at least 48 hours because perioperative mortality falls from 10% at 6 hours after onset to 5% if the operation is delayed at least 48 hours.
4. Most patients (80%) having coronary artery bypass grafting in the USA are either overweight or obese. In women, but not in men, 30-day mortality is higher in patients with a body mass index ≥30 kg/m^2 compared with patients with a body mass index <30 kg/m^2; mortality is particularly higher in those with a body mass index >40 kg/m^2. Roberts suggested that coronary bypass operation should be avoided in most patients with a body mass index >40 kg/m^2.
5. Patients having coronary bypass, of course, should be on one or more lipid-modifying drugs, aspirin, and probably an angiotensin-converting enzyme inhibitor or an angiotensin receptor blocker, unless the drugs are contraindicated.
6. Roberts believes aortic valve replacement for aortic stenosis is contraindicated in the absence of symptoms, but not so with either pure aortic regurgitation or pure mitral regurgitation.
7. In general, mitral valve repair is better than replacement for pure mitral regurgitation secondary to mitral valve prolapse. Whether repair is more advantageous than replacement for ischemic mitral regurgitation is less clear. For patients with ischemic mitral regurgitation, the decision to repair should be made preoperatively and not when the patient is under general anesthesia because the degree of regurgitation is frequently underestimated in that circumstance.
8. The added technical complexity of implanting stentless bioprosthetic valves does not justify their use over regular bioprostheses because their hemodynamic profiles are similar.

PROVIDING HIGH-QUALITY CARE IN A COST-CONSTRAINED ENVIRONMENT

J. Sanford Schwartz, MD, Professor of Medicine and Health Management and Economics, School of Medicine and The Wharton School, University of Pennsylvania, Philadelphia, Pennsylvania

1. The medical care controversy in the USA centers on 3 factors: *access*, *cost*, and *quality*. Our system can readily support any 2 but not all 3. If everyone had access to the system (now 45 million have no medical insurance), and if the quality remained high, the cost would be prohibitive. If quality was sacrificed, then we could afford access to the system by everyone. But, all Americans demand high quality. Schwartz suggested that if all Americans could settle for "good" medical care rather than the "best" medical care, we could afford that.

2. When evaluating medical care, at least 4 factors must be taken into account: safety (are side effects acceptable?), efficacy (can it work?), effectiveness (does it work?), and efficiency (is there sufficient value?).
3. Because wants and needs exceed resources, choices must be made. Medical dollars might best be applied to achieve the most gain for the most people. This theoretical goal, however, is unacceptable in the USA.
4. The rate of medical care inflation rises faster than that of general inflation for the following reasons:
   a. Medical care is *inefficient*, i.e., wasteful of time, energy, and materials, and the intended result of therapy is too often not achieved. Therapy, in general, is based on results from clinical trials where follow-up is good and patients take the medicines as prescribed. This net benefit under optimal conditions is called efficacy, but clinical practice is not efficacious but simply effective, i.e., achieves net benefit under average but not ideal conditions.
   b. Because people now live longer than in the past, chronic illness in the population is more frequent, more medical care is required, and present-day therapy, which is so much better than in the past, further prolongs life.
   c. Defensive medicine—ordering unnecessary tests to protect from possible litigation—is practiced.
   d. The newer drugs and sophisticated technology are very expensive.
   e. Because a third party (insurer, employer, government) pays most medical bills, individuals want the best because to them it is free. The American view of health care is, "Everyone deserves the best health care as long as someone else pays."
5. At least 3 types of cost analyses have to be considered: 1) the type of analysis—either cost effectiveness or cost benefit; 2) the point of view of the analysis—society, patient, payer, provider; 3) the types of costs and benefits included—direct (medical care), indirect (out of work), intangible (pain and suffering). The benchmark in determining medical usefulness in the USA is $60,000 per year of life saved. To put this in perspective, the incremental cost per additional life-year saved for coronary artery bypass surgery vs medicine for severe angina pectoris and triple-vessel coronary disease is estimated to be $13,000, whereas giving nonionic vs ionic contrast for low-risk patients is $220,000 per additional life-year saved.

ESTROGENS, ANTIOXIDANTS, BODY WEIGHT, AND CORONARY ARTERY DISEASE

Margo A. Denke, MD, Professor, Department of Internal Medicine, Center for Human Nutrition, University of Texas Southwestern Medical Center, Dallas, Texas

1. It is excess caloric intake and not a lack of physical activity that explains obesity. Caloric restriction is the only way to lose >5 lb per year. Energy is never destroyed; it is either transferred or stored.
2. An intake of at least 1200 calories a day is needed to prevent the basic metabolic rate from falling.
3. The amount of nonexercise activity (thermogenesis) that an individual exhibits may explain why some individuals who seem to eat all they want do not gain weight while others do. Obese people move only their eyes and mouth; the nonobese are fidgeters.
4. Although the weight-loss goal is to obtain and maintain ideal body weight, few ever reach that goal. Only a 5% reduction in body weight, however, reduces blood pressure, blood lipids, and blood glucose and therefore decreases atherosclerotic and hypertensive events.
5. Behavior modification should be the key goal in attempts to help patients achieve weight loss. Important components of any weight-loss plan include setting realistic goals; teaching patients how to record and self-monitor dietary intake and physical activity; and educating them about diet and avoidance of situations where overconsumption is likely.

MANAGING ATRIAL FIBRILLATION

Robert J. Myerburg, MD, Director, Division of Cardiology, Department of Medicine, University of Miami School of Medicine, Miami, Florida

1. Therapy of atrial fibrillation (AF) is dependent on a number of factors:
   a. Length of time that AF has been present (<48 hours, days to weeks, or months to years)
   b. Whether the present episode of AF is the first episode or one of many
   c. Whether underlying structural heart disease is present and, if so, the type of heart disease present
   d. If heart disease is present, whether heart failure is a consequence
   e. The age of the patient, specifically whether ≤65 or >65 years of age
   f. Whether the goal of therapy is rate control or rhythm control
   g. Whether therapy should be electrical cardioversion alone, an antiarrhythmic agent alone, electrical cardioversion plus an antiarrhythmic agent, or no therapy
   h. If an antiarrhythmic agent is to be given, the route to be used (intravenous or oral)
   i. Whether warfarin sodium should be given and, if so, over what period of time and at what dose
2. Not all patients with first-time AF require antiarrhythmic therapy and/or cardioversion because 50% of these patients convert spontaneously within 24 hours and another 25% convert within 72 hours.
3. Patients with AF, irrespective of whether hemodynamic compromise occurs, require rate control (i.e., the ventricular rate) or rhythm control (i.e., conversion to sinus rhythm) or both.
4. Most effective electrical cardioversion requires a minimum shock energy of 200 joules and, more commonly, 300 or 360 joules.
5. In patients without structural heart disease and without hemodynamic compromise, electrical cardioversion can be done safely as an outpatient procedure; if underlying structural heart disease is present, cardioversion (either by antiarrhythmic drug or electrical cardioversion or both) should be performed in the hospital.
6. Patients ≥65 years of age and those with structural heart disease require warfarin therapy, unless contraindicated, before,

at the time of, and after cardioversion with the goal of an international normalized ratio ≥2 but <4.
7. Among patients ≥65 years of age, a rhythm-control strategy has no survival benefit over a rate-control strategy. These patients need warfarin therapy but not antiarrhythmic agents or electrical cardioversion unless there is hemodynamic compromise.
8. All antiarrhythmic agents have potential proarrhythmic consequences.
9. Procainamide and amiodarone are available in both intravenous and oral forms, and ibutilide is available only in intravenous form. The other arrhythmic agents (dofetilide, flecainide, sotalol, and propafenone) are available in oral form only, at least in the USA.
10. For rhythm control for patients without structural heart disease, Myerburg prefers flecainide, propafenone, or sotalol; for those with systemic hypertension, propafenone, disopyramide, or flecainide; for those with established coronary heart disease, sotalol or dofetilide; and for those with definite heart failure, amiodarone or dofetilide.

EVIDENCE-BASED MANAGEMENT OF VALVULAR HEART DISEASE

Robert O. Bonow, MD, President, American Heart Association; Chief, Division of Cardiology, Northwestern University Medical School, Chicago, Illinois

1. Most patients with aortic stenosis should wait until symptoms appear before having valve replacement. Asymptomatic patients with aortic stenosis might require valve replacement when objective evidence of left ventricular systolic function appears, when the systemic blood pressure fails to increase during exercise testing, or when evidence of myocardial ischemia, high-grade ventricular arrhythmias, severe left ventricular hypertrophy, or severe obstruction appears (valve area <0.6 cm^2).
2. In contrast to patients with aortic stenosis, patients with pure (no element of stenosis) aortic regurgitation may need valve replacement before symptoms appear. When left ventricular dimensions become >55 mm in peak systole or when the left ventricular ejection fraction falls on serial studies to <40%, valve replacement is warranted. Patients with aortic regurgitation, however, usually develop symptoms about the same time that left ventricular dysfunction appears.
3. Afterload-reducing agents (angiotensin-converting enzyme inhibitors, nitroprusside, hydralazine, nifedipine) delay progression of aortic regurgitation, but these agents should be used only in asymptomatic patients with normal left ventricular function.
4. Proper timing of mitral valve surgery in patients with pure mitral regurgitation remains difficult. The surgery is indicated in patients with substantial symptoms; asymptomatic or mildly symptomatic patients who develop atrial fibrillation; asymptomatic patients with a left ventricular ejection fraction <60% or those with a progressive decline in left ventricular ejection fraction; asymptomatic patients with left ventricular systolic dimensions ≥45 cm^2; and asymptomatic patients with moderate to severe pulmonary hypertension.
5. Mitral valve repair or chordal-sparing mitral valve replacement should be performed when possible because both preserve the subleaflet apparatus and improve postoperative survival.

HYPERTROPHIC CARDIOMYOPATHY AND COMMOTIO CORDIS

Barry J. Maron, MD, Director, Division of Cardiovascular Research, Minneapolis Heart Institute Foundation, Minneapolis, Minnesota

1. Patients with hypertrophic cardiomyopathy (HC) presenting to tertiary care centers have an annual mortality rate of about 6% and represent a group of patients with more severe forms of HC, refractory to medical therapy. The annual mortality rate of patients in the general population is closer to 1%.
2. Young patients with severe forms of HC tend to die suddenly. In contrast, older patients with HC more commonly die of stroke or heart failure.
3. Sudden death in patients with HC is more likely in those with previous episodes of cardiac arrest; those in whom another family member died suddenly; those with recurrent syncope; those with repeated episodes of nonsustained ventricular tachycardia; and those with a ventricular septum >30 mm in thickness.
4. Patients with worsening dyspnea or overt heart failure with superfunctioning left ventricles require medical therapy (beta-blocker or calcium antagonist); those with demonstrated left ventricular outflow obstruction usually require alcohol septal ablation or myotomy-myectomy (Morrow procedure); and those with refractory symptoms and no left ventricular outflow obstruction need to be considered for cardiac transplantation.
5. HC is the most common cause of sudden death in competitive athletes.
6. Commotio cordis, a phenomenon that occurs in structurally normal hearts, is cardiac arrest from ventricular fibrillation due to a nonpenetrating blow to the chest. Nearly all victims are under the age of 20, and most events are related to sports. This vulnerable period for the death-dealing blow to the chest corresponds to the peak or upstroke of the T wave on electrocardiogram. It is best not to hit another in the anterior chest wall, and then commotio cordis is a nonentity!