



Oklahoma Heart Institute

volume 3 • number 5 • fall 2007

UNEXPLAINED DYSPNEA:

CONSIDER PULMONARY ARTERIAL HYPERTENSION

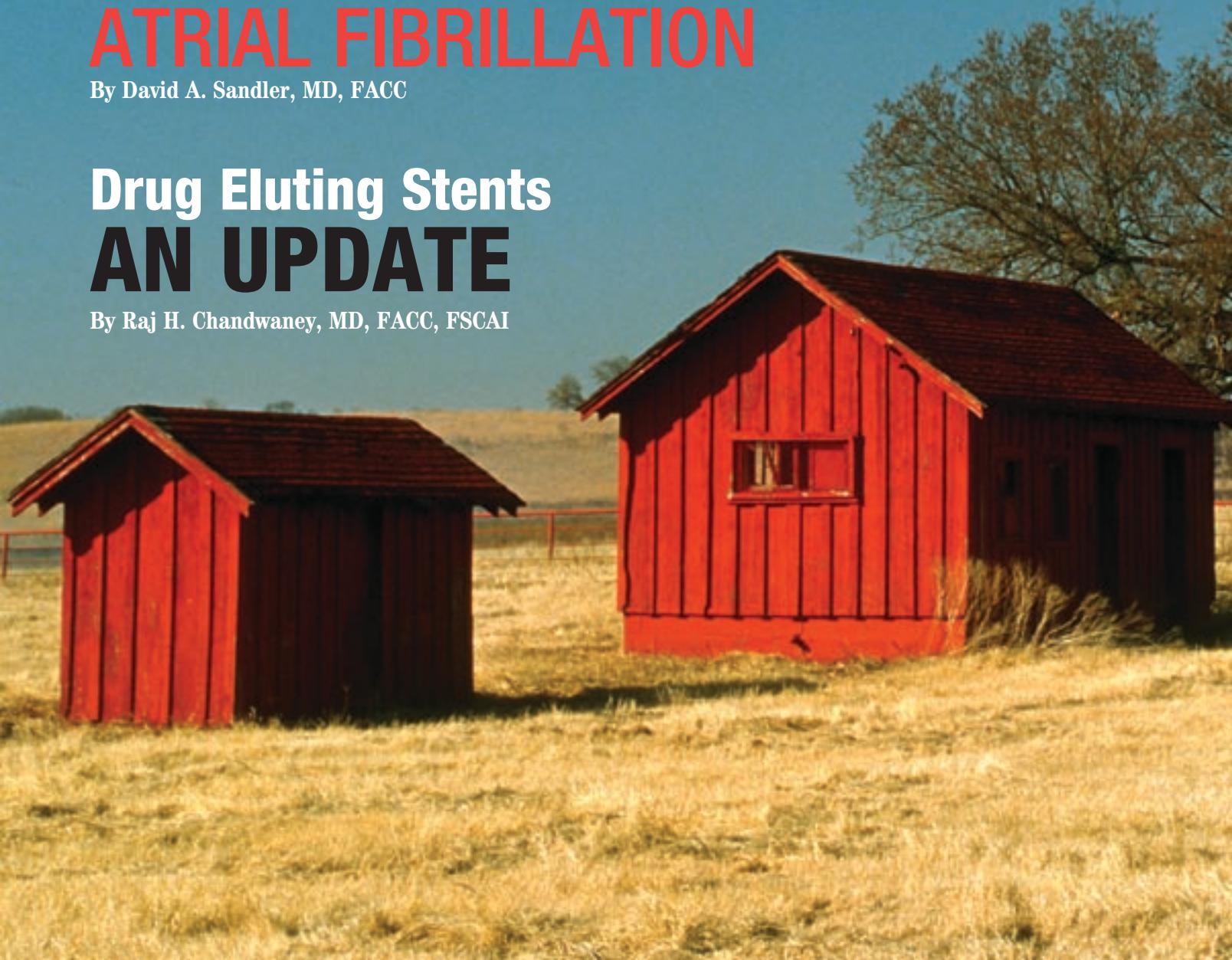
By Wayne N. Leimbach, Jr., MD, FACC, FSCAI, FCCP, FAHA

ABLATION FOR ATRIAL FIBRILLATION

By David A. Sandler, MD, FACC

Drug Eluting Stents AN UPDATE

By Raj H. Chandwaney, MD, FACC, FSCAI



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AT SOUTHPOINTE**

9228 S. Mingo

Suite 200

Tulsa, OK 74133

Phone: 918.592.0999

Fax: 918.878.2499

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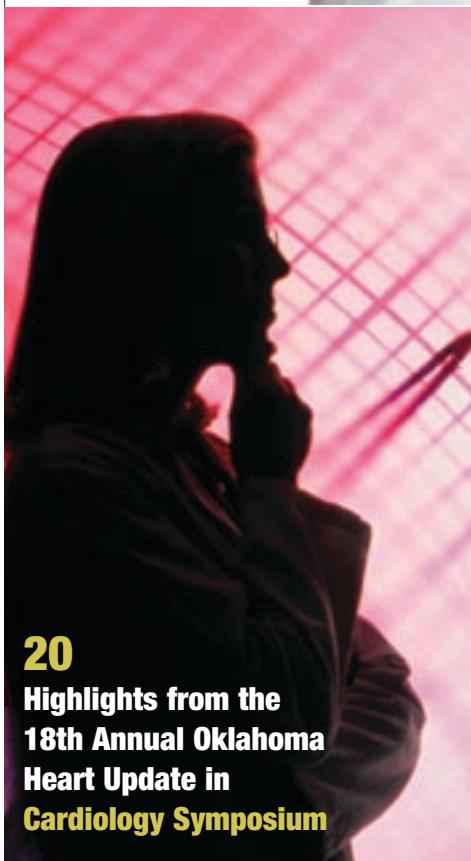
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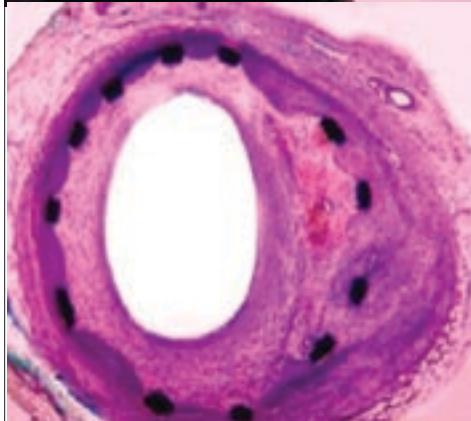
**Oklahoma
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Institute**

The *Oklahoma Heart Institute* magazine is mailed directly to referring physicians and other referring health care professionals in the Tulsa area and is also available in our patient waiting areas.

Cover photo by Rick Stiller



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18th Annual Oklahoma
Heart Update in
Cardiology Symposium**



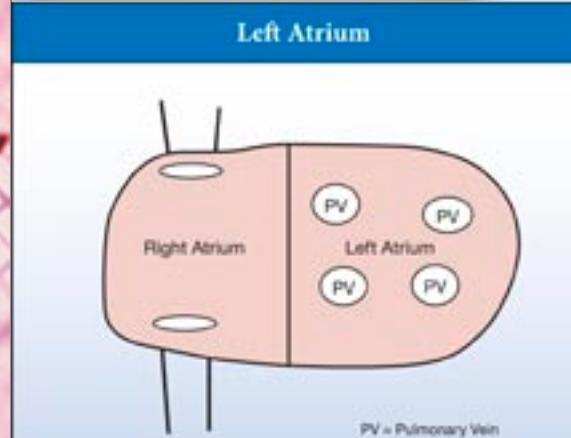
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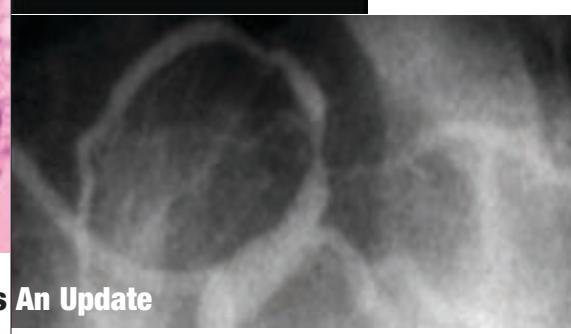
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To Our Readers



THE FIELD OF CARDIOLOGY continues to evolve at a rapid pace. For common disease states, such as atrial fibrillation, the development of very effective new techniques can sometimes eliminate the problem for many patients. In this issue of Oklahoma Heart Institute magazine, Dr. David Sandler, an electrophysiologist at Oklahoma Heart Institute, discusses ablation therapy for atrial fibrillation, a therapeutic option that is being chosen much more frequently.

In addition, for uncommon but severe disease conditions, such as pulmonary arterial hypertension, the emergence of effective therapies can improve the quality of life for those patients affected with this previously untreatable condition.

Controversy continues to provoke intense analysis of current treatment algorithms in cardiology. Dr. Raj Chandwaney, an interventional cardiologist with Oklahoma Heart Institute, reviews the issues surrounding coronary stenting and the concerns regarding the use of bare metal stents versus drug eluting stents.

Highlights from the 18th Annual Oklahoma Heart Update in Cardiology Symposium, Late Breaking Clinical Trials session are presented, including the controversial COURAGE Trial. This trial looked at optimal medical therapy versus interventional therapy with angioplasty and stents for the treatment of stable coronary artery disease.

In addition, the results of the MEGA Trial and METEOR Trial highlight the controversy regarding whether risk factor modification prevention algorithms should be expanded to include low risk patients.

We hope you enjoy these articles and welcome any comments or suggestions regarding magazine content.

Sincerely,

A handwritten signature in cursive script that reads "Wayne Leimbach".

Wayne N. Leimbach, Jr., MD





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Introducing 4 Easy Ways To Live Longer

According to the American Heart Association, 64% of women and 50% of men who die suddenly of Coronary Heart Disease had no previous symptoms.

Even if you have no signs or symptoms, a simple screening by trained experts in cardiovascular disease can detect it now, preventing future problems down the road. The cost is low. The tests simple and fast. The results... well, aren't you worth it?

1 Carotid Artery Evaluation

Strokes rank 3rd among all causes of death behind diseases of the heart and cancer. To assess your risk for stroke, an ultrasound probe is placed on your neck to screen for blockages in your carotid arteries which supply blood to the brain. This is also a marker of heart attack risk.

15 minutes, \$40

2 Cardiac Function Evaluation

To analyze cardiac function and calculate your Ejection Fraction (the amount of blood your heart is able to pump), an ultrasound probe will be positioned at various locations on your chest.

15 minutes, \$40

3 Abdominal Aorta Evaluation

Most abdominal aneurysms are asymptomatic. They're the 10th leading cause of death in males over 55. To screen for aneurysm, an ultrasound probe is used to analyze your abdominal aorta.

15 minutes, \$40

4 Ankle/Brachial Index

Blood pressures are obtained from your legs and arms to evaluate whether you may have peripheral artery disease. It not only assesses circulation to the legs, but also is a marker of heart attack risk.

15 minutes, \$40

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Simple exercises
and common sense
can help prevent
Repetitive Stress Injuries

ErgAerobics

By Chris Hansen



Four things employees and employers need to do to help themselves...

- 1—Have good posture
- 2—Have a good workstation set up
- 3—Perform one minute of stretching exercises at the computer each hour
- 4—Take regular breaks

ErgAerobics

Physical therapist Perry Bonomo's private practice in New Milford, N.J., had become a revolving door for secretaries and office workers who would come in suffering from the same ailments: sore wrists, pains in the neck, achy backs.

"So many people were suffering from these same problems," Bonomo said.

The problem? Repetitive Stress Injuries (RSI). Or more specifically, Computer Induced Repetitive Stress Injuries (CIRSI). Herniated lumbar or cervical discs, forward head posture and Carpal Tunnel Syndrome, which occurs in the wrists, all the result of sitting in front of a computer for a significant amount of time each day at work.

"It's a white collar epidemic in our nation," Bonomo claimed.

And it's not just affecting the workers.

According to the United States Department of Labor, repetitive stress injuries are a staggering \$100 billion a year problem for corporate America, with a large portion CIRSI related.

Carpal Tunnel Syndrome is by far the most common and expensive culprit. Not only does the USDL conclude that Carpal Tunnel Syndrome is the chief occupational hazard of the 1990s, but the National Council of Compensation Insurance claims the average compensation received by a victim of Carpal Tunnel Syndrome is \$33,000.

Carpal Tunnel Syndrome occurs when the wrists are exposed to repetitive strain. The tissues surrounding the tendons become so enlarged, they compress the median nerve, which runs through the carpal tunnel, a passage in the wrist.

The results can vary from reduced muscle control in the wrist, loss of the wrist's nervous function, diminished grip strength, numbness, tingling, pain, and a reduced ability to grasp, pinch and manipulate objects with the hand.

The Bureau of Labor and Statistics and the National Institute of Occupational Safety and Health also provide statistics that give insight as to how RSIs adversely affect workers. Carpal Tunnel Syndrome is the No.1 reported medical problem accounting for 50 percent of all work-related injuries; 36 percent of all Carpal Tunnel Syndrome patients require unlimited medical treatment; women are twice as likely to develop Carpal Tunnel Syndrome than men; and women, which account for 45 percent of the American work force, suffer from nearly two-thirds of all work-related RSIs.



And to think most CIRSI's can be prevented by just some common-sense practices: sit up straight, don't slouch, don't sit so close to the screen, have a clean desk and don't

forget to exercise.

In no particular order of importance, Bonomo said the four things employees and employers need do to help themselves is No. 1, have good posture; No. 2, have a good workstation set up; No. 3, perform one minute of stretching exercises at the computer each hour; and No. 4, take regular breaks.

POSTURE

The way you position yourself while sitting at a computer is vital to preventing neck, arm, leg and back injuries.

According to Bonomo, poor posture, such as slouching, multiplies the already stressful forces placed on the spine while sitting, and can potentially cause a herniated lumbar disc and overstretch the postural muscles which support your spine.

Because computer users often

causes the muscles at the base of the head and neck to tighten and restrict blood flow. This can lead to headaches, neck pains and potentially, pain down through the arms and hands.

Poor posture can also lead to rounded shoulders, which is a result of the shoulders not being aligned directly over the hips and directly below the ears. Rounded shoulders can cause undo stress on the shoulder tendons and cause a tightening of the upper arm muscles.

For good posture, Bonomo recommends that when sitting at a computer workstation, always try to sit an inch taller than normal. Align your ears directly over your shoulders. Align your shoulders directly over your hips. Position your head evenly between both shoulders, not tilted in one direction or the other. When looking down, your head should be positioned over your neck and not in front of your shoulders.

ERGONOMICS

Good posture is hard to maintain if the computer monitor isn't positioned directly in front of you, or if you have to be constantly reaching for items on your desk. Everything in your workstation must be positioned to benefit you.

Starting with the desk, make sure you have one large enough to hold the monitor, keyboard, mouse and all necessary documents.

When positioning the monitor, make sure the top edge is at eye level, or no more than six inches below. It should be placed directly in front of you at approximately one arms length.

An adjustable chair with a lumbar support pad or roll is recommended. This gives you the ability to swivel, instead of stretch, for out of reach objects. Make sure there is enough

"It doesn't take a brain surgeon," Bonomo admitted. **"It's just a matter of people doing the right things while at their computer. Our whole goal is just to prevent these injuries from happening."**

strain to see their monitor, they can develop what is called forward head posture. It occurs when the head is positioned in front of the shoulders and not directly above them. This



space underneath the chair to bend and straighten the knees comfortably.

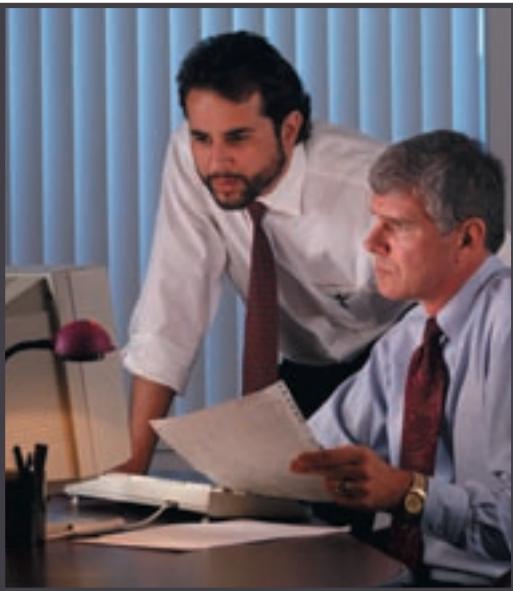
A padded strip in front of the keyboard is also highly recommended by Bonomo. This will help to keep your wrists straight while typing, which decreases the chance of getting

little bit lower than your elbows and your elbows are bent an inch in front of your trunk. Put your wrists in a neutral position (not bent up or down).

After that, Bonomo said, just relax.

Studies have shown that companies can ergonomically modify workstations for a cost ranging from

It's also important to remember, Bonomo said, that doing all four preventative measures will also work to reduce fatigue and improve overall efficiency and effectiveness at work.



Carpal Tunnel Syndrome.

"Imagine your wrists as drinking straws," Bonomo explained, "when a straw is bent, it becomes harder to suck the liquid through. Same goes for your wrists. When they are bent, it pinches and restricts the blood flow."

With all the equipment positioned around you, it is just as important to position yourself correctly.

First, place your feet flat on the floor or a footrest support. Slightly arch your low back with the support of a lumbar cushion or pillow. Move your head back on top of your spine so that your ears are directly over your shoulders and hips. Let your arms rest comfortably at your sides and align your shoulders directly above your hips. Let your forearms rest on padded armrests at the height where your wrists are a

\$100 to \$300 per employee. Doing this can reduce the risk of Carpal Tunnel Syndrome by nearly 70 percent.

EXERCISES

Along with fellow physical therapist Daniel Seidler, Bonomo has written a book titled "*ErgAerobics: Why Does Working @ My Computer Hurt So Much?*" Included in the book are five simple exercises that can be performed right at a workstation in a matter of minutes.

To prevent lumbar disc herniations, which stem from sitting for an extended period of time, stand up, and with your hands on your hips, slowly lean back.

Or to increase blood flow to your hands and relieve tension in your wrists, rest your arms on your arm-

rests, and with palms facing downward, slowly open and close your hands.

To help prevent the onset of Carpal Tunnel Syndrome, straighten your arm out in front of you as if you were pointing at something at shoulder height. Use your other hand to bend back your wrist so your fingers point towards the ceiling. This exercise stretches the wrist flexors and finger flexors and increases circulation through the wrist and hand.

After doing some exercises, stand and take a quick break and allow the muscles to rest.

If it seems too simple, it's because it is.

"It doesn't take a brain surgeon," Bonomo admitted. "It's just a matter of people doing the right things while at their computer. Our whole goal is just to prevent these injuries from happening."

It's also important to remember, Bonomo said, that doing all four preventative measures will also work to reduce fatigue and improve overall efficiency and effectiveness at work.

But do all four, not just one or two, he reminds.

"It's the combination that works to prevent these injuries," Bonomo said. "Just because your company goes out and buys you the perfect chair, it won't prevent Carpal Tunnel if you still type with your wrists bent all day or your computer monitor is positioned incorrectly."

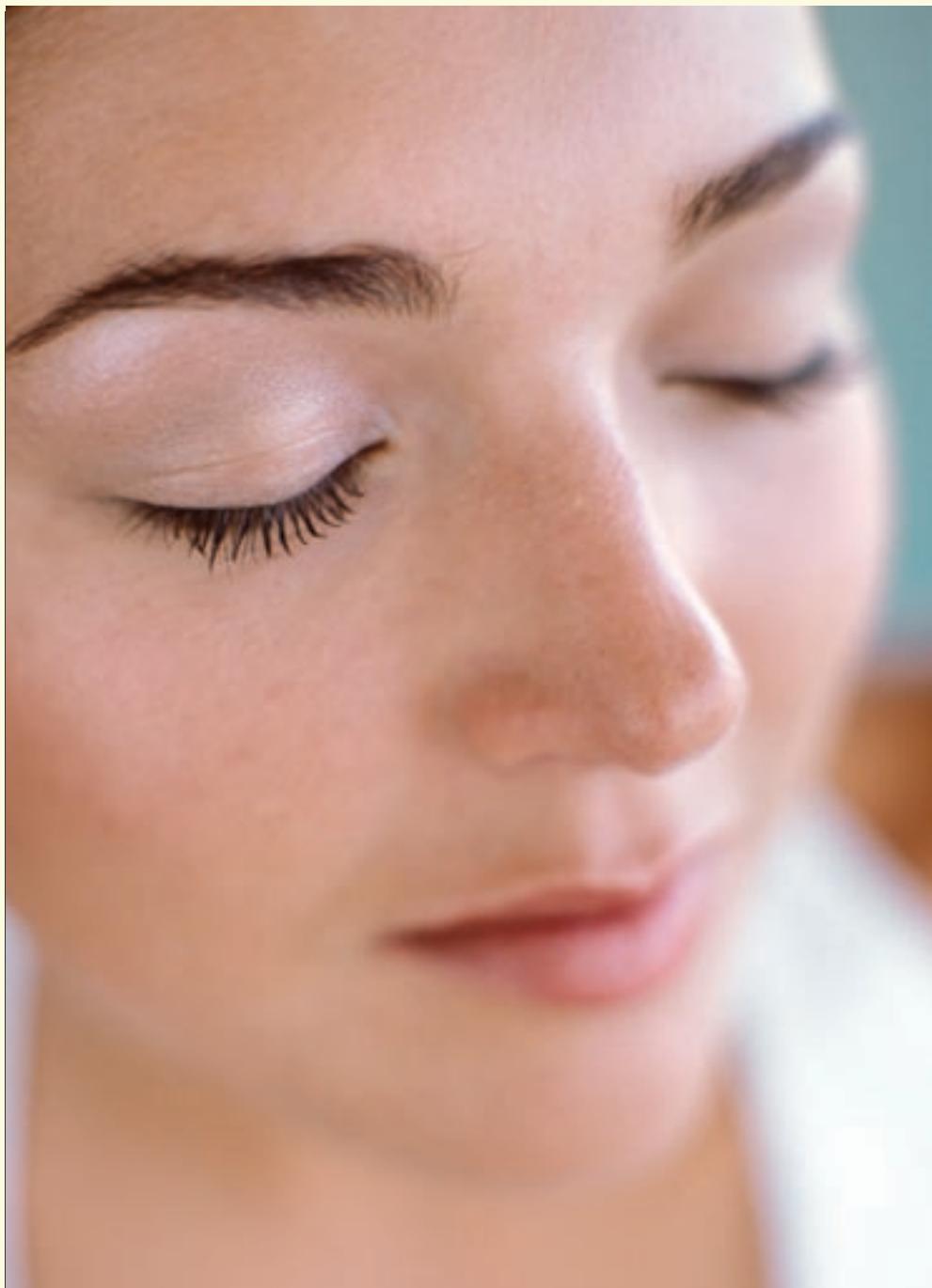
RSIs are considered to be micro-trauma injuries, Bonomo said. In other words, they occur from gradual wear and tear on the body from everyday activities. It may take several months or years of poor posture or a repetitive motion before you feel any pain. And unless the proper preventative measures are taken, the pain could last a lifetime.

Unexplained Dyspnea:

CONSIDER PULMONARY ARTERIAL HYPERTENSION

Pulmonary arterial hypertension (PAH) is a progressive, complex disease usually presenting with symptoms of dyspnea and fatigue. Until very recently, treatment strategies were limited and prognosis remained very poor for patients with pulmonary arterial hypertension. The natural history of idiopathic pulmonary arterial hypertension was described by the National Institutes of Health registry performed at 32 clinical centers during the 1980s. The median survival was 2.8 years with one-, three-, and five-year survival rates of 68 percent, 48 percent, and 34 percent, respectively. Many physicians today still associate the diagnosis with a hopeless condition. However, significant advances have been made in our understanding of the disease process. New treatment strategies are now being developed and some have recently become clinically available. It is therefore important for physicians to be aware of these new treatment options which may significantly help their patients with pulmonary arterial hypertension.

Pulmonary arterial hyperten-



sion (PAH) is characterized by continuous high blood pressure in the

pulmonary arteries. Pulmonary arterial hypertension may be idiopathic



or it may be associated with other conditions, such as connective tissue diseases. Approximately 35 percent of scleroderma spectrum disease patients will develop pulmonary arterial hypertension. This is particularly significant, since the development of PAH in patients with scleroderma spectrum diseases significantly shortens their lives. The World Health Organization

are also associated with pulmonary arterial hypertension.

The hallmark of pulmonary arterial hypertension is hypertrophy, fibrosis, and cellular proliferation of both the endothelial and smooth muscle cells in the pulmonary vasculature. This results in inflammation and vasoconstriction. The plexiform lesion is the hallmark of pulmonary artery

hypertension.

There are three phases of pulmonary arterial hypertension. During the pre-symptomatic or compensated phase, pulmonary artery pressures are silently rising and the patient remains asymptomatic. During this time, cardiac output is maintained. In the symptomatic or

decompensating phase, cardiac output starts to fall as pulmonary artery pressure continues to rise and right atrial pressure starts to rise. Finally, in the decompensated phase, cardiac output falls; the patient develops

fatigue, severe shortness of breath, and evidence of right-sided heart failure.

Idiopathic pulmonary hypertension is uncommon, but physicians need to consider the diagnosis when seeing patients with unexplained dyspnea. The female to male ratio is about 1.7 to one. The mean age at diagnosis was 37 years in the NIH national registry. Therefore, this is a disease

that affects people in their prime. Dyspnea is the most common presenting symptom. It is almost universally present during the course of the illness. The patients also experience fatigue, chest pain, near syncope, or syncope, and ultimately they develop signs of right-sided heart failure.

The echocardiogram remains the best screening test for pulmonary arterial hypertension. The echocardiogram may be able to estimate pulmonary artery pressures using Doppler evaluation. In addition, right atrial enlargement and right ventricular hypertrophy may occur. There may be flattening of the inter-

Figure 1
**WHO Classification
for Pulmonary HTN**

- I. Pulmonary Arterial Hypertension
- II. Pulmonary Venous Hypertension
- III. Pulmonary Hypertension Associated with Disorders of the Respiratory System or Hypoxemia
- IV. Pulmonary Hypertension Caused by Thrombotic or Embolic Disease
- V. Pulmonary Hypertension Caused by Diseases Affecting Pulmonary Vasculature

classification for pulmonary hypertension includes five groups: group 1: pulmonary arterial hypertension; group 2: pulmonary venous hypertension; group 3: pulmonary hypertension associated with disorders of the respiratory system or hypoxemia; group 4: pulmonary hypertension caused by thrombotic or embolic disease; and group 5: pulmonary hypertension caused by diseases affecting pulmonary vasculature, such as vasculitis (see Figure 1). It is important to differentiate group 1 from pulmonary venous hypertension, which is the most common form of pulmonary hypertension. Pulmonary venous hypertension is often seen with left ventricular heart failure. Pulmonary arterial hypertension includes idiopathic pulmonary hypertension, familial pulmonary hypertension, and pulmonary hypertension associated with collagen vascular disease, congenital systemic pulmonary shunts, HIV infections, and some toxins and drugs. Some hemoglobinopathies

The echocardiogram remains the best screening test for pulmonary artery hypertension

Figure 2
PAH Definition on Right Heart Catheterization

- Increased mPAP:
 >25 mm Hg at rest, or
 >30 mm Hg during exercise
- PVR: >3 Wood units
- Normal PCWP: <15 mm Hg

ventricular septum and a dilated pulmonary artery.

Pulmonary arterial hypertension is diagnosed by right heart catheterization (Figure 2). Increased mean pulmonary artery pressures greater than 25mm at rest or greater than 30mm during exercise defines pulmonary hypertension. Pulmonary vascular resistances greater than three Wood Units are also associated with pulmonary

arterial hypertension. In order to make the diagnosis of pulmonary arterial hypertension, the pulmonary capillary wedge pressure needs to be less than 15mmHg. In

such as bosentan (Tracleer) and ambrisentan (Letairis). Finally, the prostacyclin pathways provide the rationale for the use of prostacyclin analogs such as epoprostenol (Flolan), treprostinil (Remodulin), and iloprost (Ventavis) (Figure 3)

Recent clinical trials have demonstrated that these newer agents do provide improvement in quality of life for these patients. The

Two studies evaluating the efficacy of the endothelin receptor antagonist of bosentan demonstrated that six minute walk times increase significantly over 12 weeks in patients randomized to bosentan, as compared to those randomized to placebo. In the BREATH-1 trial, the 144 patients randomized to bosentan demonstrated an increase in their six minute walk distance of 44 meters, which was significantly greater than in the 69 patients randomized to placebo. The placebo group actually demonstrated a small deterioration over the 16-week study (Figure 4).

Clinical trials demonstrated an improvement in functional classification in 42-43 percent of patients receiving the endothelin antagonist bosentan. Only two percent of patients showed a worsening of their clinical status while on bosen-

Figure 3 FDA-Approved Therapeutic Options for PAH

- Prostanoids
 - Epoprostenol (Flolan)
 - Treprostinil (Remodulin)
 - Iloprost (Ventavis®) inhalation solution
- Endothelin Receptor Antagonists
- PDE-5 Inhibitors

situations where patients have an elevated pulmonary capillary wedge pressure of greater than 15, the pulmonary arterial hypertension is probably secondary to elevated left ventricular end diastolic pressures, which is associated with pulmonary venous hypertension.

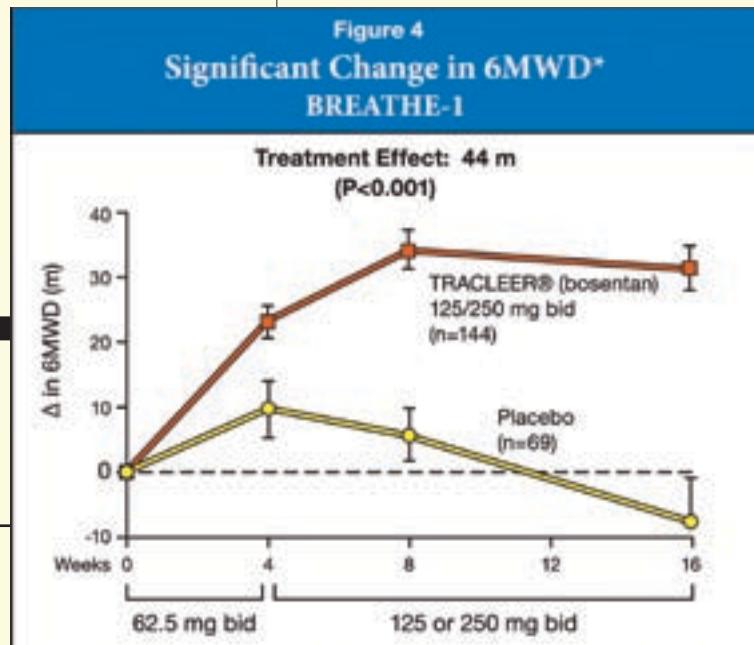
Research over the last decade suggests that there may be three major pathways active in the pulmonary vasculature involved in

use of the prostacyclin analogs requires the patients to receive either intravenous infusions, continuous subcutaneous infusions, or frequent inhalation treatments six to nine times a day. Because of

This is a disease that affects people in their prime.

the development and progression of pulmonary arterial hypertension: the nitric oxide pathways, the endothelin pathways, and the prostacyclin pathways. These three pathways interact with each other and also provide potential targets for therapeutic agents. The phosphodiesterase type 5 (PDE-5) inhibitors enhance nitric oxide dependent cGMP-mediated pulmonary vasodilatation by inhibiting the breakdown of cyclic cGMP by PDE-5. The endothelin pathway provides the rationale for the use of endothelin receptor antagonists,

the significant logistical problems with the continuous infusion and frequent inhalation therapies, these agents are used for patients with the most advanced disease. However, the endothelin antagonist and the phosphodiesterase inhibitors can be taken orally and now provide patients with much easier treatment options.



tan. In addition, studies evaluating hemodynamics before and during treatment with bosentan demonstrated an increase in cardiac index, along with a decrease in mean pulmonary artery pressures during the treatment period. In addition,



patients randomized to bosentan in the BREATHE-1 Trial demonstrated a 71 percent relative risk reduction for the secondary end point of clinical worsening as compared to the placebo patients. During the 28 week treatment period, 89 percent of the bosentan patients remained free of evidence of clinical worsening, as compared to 63 percent of the placebo treated group. This not only illustrated the benefits seen with treatment with bosentan, but also highlighted the progressive nature of pulmonary artery hypertension with

pregnancy checks are routinely done.

Phosphodiesterase-5 inhibitors are also being shown to be beneficial in patients with pulmonary arterial hypertension. Sildenafil has been released under the name of Revatio. The patients randomized to sildenafil did show improvements in exercise walk time and a decreased chance of clinical worsening over the study period.

The relative role of the endothelin antagonist and phosphodiesterase-5 inhibitors is not clear. At this

time, there is much greater clinical data for the endothelin receptor antagonist bosentan than there is for the use of sildenafil in pulmonary arterial hypertension. It is also possible that combination therapy may be the pre-

ferred option for these patients in the future.

Patients who have class IV pulmonary arterial hypertension or who have continued to deteriorate despite endothelin receptor antagonist and phosphodiesterase type 5 inhibitors, will need to be treated with the prostacyclin analogs. The greatest clinical experience exists for epoprostenol (Flolan). The use of this drug, however, is limited by the fact that it has to be given as a continuous IV infusion. It has a very short half-life, and disruption of the infusion can cause rapid deterioration in the patients' clinical status. Treprostinil (Remodulin) has a longer half-life and can be given both by I.V. and subcutaneously. Some patients do have significant problems with injection site reactions with the treprostinil.

Recently, iloprost (Ventavis) has been approved for inhalation therapy. Patients need to take six to nine inhalation treatments daily during the waking hours. The prostacyclin analogs provide significant symptomatic improvement even in patients with advanced pulmonary arterial hypertension.

Because pulmonary arterial hypertension is often diagnosed late in the course of the disease, and because of its poor prognosis when left untreated, it is imperative that physicians now begin to look for the diagnosis earlier in patients with unexplained dyspnea. This is particularly true since there are now new treatment strategies, which can slow down the rate of deterioration radically and improve the quality of life for these patients. Therefore, idiopathic pulmonary hypertension and pulmonary artery hypertension associated with connective tissue diseases is no longer a hopeless diagnosis. Physicians who are unsure about the diagnosis should screen their patients with echocardiograms and, if still unclear, then refer their patients for a right heart catheterization. Clinical centers which deal with patients with pulmonary hypertension are available throughout the United States. Referrals to these centers provide patients access to newer treatment strategies, which can radically improve the prognosis for these patients (Figure 5).

- PAH is characterized by vascular proliferation, hypertrophy, and fibrosis, leading to hemodynamic and right ventricular abnormalities
- PAH progresses rapidly and has poor prognosis
- Echocardiogram is good screening tool for PAH but RHC is required for confirmation of diagnosis
- Endothelin, prostacyclin, and nitric oxide are thought to be key mediators in PAH and are key targets for therapy

placebo therapy. Two year survival data for two clinical randomized clinical trials using bosentan demonstrated that 84 percent of the patients were still alive at two years.

It should be noted that bosentan can be associated with potential liver toxicity. Bosentan can cause at least a three-fold elevation of liver function studies (ALT and AST) in about 11 percent of patients. 1.8 percent of patients treated with bosentan will need to have therapy discontinued due to hepatic function abnormalities. For this reason, patients receiving bosentan must have their liver function studies checked monthly.

In addition, bosentan carries a very high potential for major fetal defects. Therefore, women of child-bearing age must be counseled on the use of two forms of birth control if they are to be considered for therapy. They must also be counseled on the high risk of fetal abnormalities if they were to become pregnant and

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Dr. Leimbach is a subspecialist in interventional cardiology, including cardiac catheterization, coronary angioplasty, and related interventional procedures such as stents, atherectomy, laser, intravascular ultrasound imaging, and direct PTCA for acute myocardial infarction.

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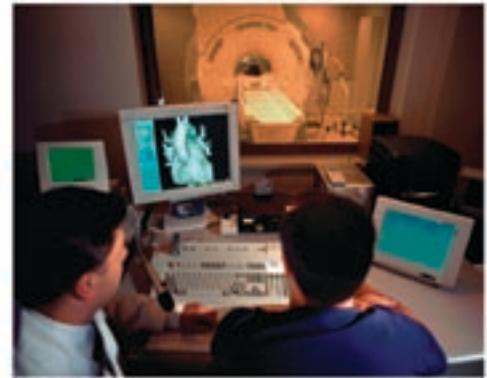


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- Peripheral Arterial Ultrasound Studies & Duplex Imaging
- Cardiovascular Magnetic Resonance Imaging
- External Counterpulsation (ECP) Therapy
- Transcranial Doppler

Invasive Cardiology

- Cardiac Catheterization
- Coronary Angioplasty
- Atherectomy
- Rotablator Atherectomy
- Thrombolytic Therapy
- Coronary Stents
- Carotid Stenting
- Intravascular Ultrasound
- Myocardial Biopsy
- Pericardiocentesis
- Intravascular Radiation Therapy
- Peripheral Angioplasty
- Peripheral Stents
- Percutaneous PFO Closures
- Percutaneous ASD Closures

Electrophysiology

- Electrophysiology Studies
- Ablation Therapy
- Pacemaker Implantation
- Pacemaker and Lead Extraction
- Pacemaker Programming
- Pacemaker Monitoring & Clinic
- Implantable Cardioverter Defibrillator (ICD) Placement
- ICD Replacement
- ICD and Hardware Removal
- ICD Programming
- ICD Monitoring and Clinic
- Holter Monitoring and Interpretation
- 30 Day Cardiac Event Monitors
- Implantation and Interpretation of Long-term Heart Monitors
- Signal Averaged EKG's and Interpretation
- Head Up Tilt Testing and Interpretation

- Direct Current Cardioversion
- Antiarrhythmic Drug Loading and Monitoring

Metabolic Disorders

- Endocrinology
- Diabetes
- Hypertension
- Hyperlipidemia
- Thyroid
- Other Metabolic Disorders

Specialty Clinics

- Hypertension Clinic
- Adolescent & Adult Congenital Heart Clinic
- Lipid & Wellness Clinic
- Heart Failure Clinic
- Dysrhythmia & Pacer Clinic
- Same Day Appointment Clinic



Oklahoma Heart Institute

THE DOCTORS OF OKLAHOMA HEART INSTITUTE

Wayne N. Leimbach, Jr., MD, FACC, FSCAI, FCCP, FAHA

Dr. Leimbach is a subspecialist in interventional cardiology, including cardiac catheterization, coronary angioplasty and related interventional procedures such as stents, atherectomy, laser, intravascular ultrasound imaging and direct PTCA for acute myocardial infarction. He

is Chief of Cardiology at Hillcrest Medical Center, where he is also Director of the Cardiac and Interventional Laboratories at Hillcrest Medical Center. Dr. Leimbach is Co-Director of the Lipid and Wellness Clinic at Oklahoma Heart Institute. He is Director of the James D. Harvey Center for Cardiovascular Research at Hillcrest Medical Center, as well as Director of the Oklahoma Heart Research and Education Foundation. He also serves as Clinical Associate Professor of Medicine at the University of Oklahoma College of Medicine – Tulsa. Dr. Leimbach completed a Clinical Cardiology Fellowship and a Research Fellowship at the University of Iowa Hospitals and Clinics. He also completed his Internal Medicine Internship and Residency programs at Iowa, where he was selected Chief Resident in Medicine. He received his medical degree from Northwestern University in Chicago and his Bachelor of Science degree from the University of Michigan.

Board certified in Internal Medicine, Cardiovascular Disease and Interventional Cardiology

Robert C. Sonnenschein, MD, FACC, ASE, RVT

Dr. Sonnenschein specializes in echocardiography and noninvasive peripheral

vascular imaging. He is Director of Peripheral Vascular Ultrasound Imaging at Hillcrest Medical Center and Oklahoma Heart Institute and serves as Clinical Associate Professor

of Medicine at the University of Oklahoma College of Medicine – Tulsa. He completed his Cardiology Fellowship at the State University of New York Upstate Medical Center in Syracuse, where he also completed his Internal Medicine Internship and Residency programs. Dr. Sonnen-



schein received his medical degree from Rush Medical College in Chicago and his Bachelor of Arts degree from the University of Pennsylvania.

*Board certified in Internal Medicine, Cardiovascular Disease and Adult Echocardiography
Registered Vascular Technologist*

Robert E. Lynch, MD, FACC

Dr. Lynch is a specialist trained in noninvasive and invasive cardiology. He is former Chief of Cardiology at Hillcrest Medical Center, where he also has served as Chief of Medicine and President of the medical staff. Dr. Lynch is Co-Director of the Lipid and Wellness Clinic at Oklahoma Heart Institute and Director of the Executive Health Program. He is also a Clinical Assistant Professor at the University of

Oklahoma College of Medicine – Tulsa. He completed his Cardiology Fellowship, as well as his Internal Medicine Internship and Residency, at the University of Oklahoma Health Sciences Center. Dr. Lynch received his medical degree from the University of Oklahoma School of Medicine and his Bachelor of Science degree from the University of Tulsa. Before establishing his practice in Tulsa, he served as Chief of Medicine at the U.S. Army Hospital, Bangkok, Thailand.

Board certified in Internal Medicine and Cardiovascular Disease

James J. Nemec, MD, FACC

Dr. Nemec is a subspecialist in echocardiography, stress echocardiography and nuclear cardiology. He serves as Director of Nuclear Cardiology for Oklahoma Heart Institute. Dr. Nemec has served as Assistant Professor

of Internal Medicine, Division of Cardiology, at Creighton University and as Assistant Professor, Department of Radiology, also at Creighton University. He completed his Clinical

Cardiology Fellowship at the Cleveland Clinic Foundation and his Internal Medicine Internship and Residency at Creighton University. Dr. Nemec also completed a year of training in pathology at the University of Missouri, Columbia, MO. He received his medical degree from Creighton University, where he also received his Bachelor of Arts degree.

Board certified in Internal Medicine and Cardiovascular Disease

Gregory D. Johnsen, MD, FACC, FSCAI

Dr. Johnsen is an interventional cardiologist with expertise in cardiac catheterization, angioplasty and related interventional pro-

cedures, such as stents and atherectomy. He is Director of Cardiac Rehabilitation at

Hillcrest Medical Center and Director of the Hillcrest Exercise and Lifestyle Programs. He completed his Clinical Cardiology Fellowship at the University of Oklahoma – Oklahoma City,

where he then finished an extra year of dedicated training in interventional cardiology. He completed his Internal Medicine Internship and Residency training at the University of Oklahoma – Oklahoma City, where he also received his medical degree. Dr. Johnsen received his Bachelor of Science degree from Oklahoma State University.

Board certified in Internal Medicine, Cardiovascular Disease and Interventional Cardiology

Alan M. Kaneshige, MD, FACC, ASE

Dr. Kaneshige is a noninvasive cardiologist with expertise in adult echocardiography, stress echocardiography and

transesophageal echocardiography. He is past Chief of Cardiology at Hillcrest Medical Center. Dr. Kaneshige is also the Director of the Adolescent and Adult Congenital

Heart Clinic at Oklahoma Heart Institute and Director of the Congestive Heart Failure C.A.R.E. Center at Hillcrest Medical Center. Dr. Kaneshige completed his Internal Medicine Internship and Residency at Creighton University School of Medicine, where he also received his medical degree. He received a Bachelor of Science in chemistry at Creighton University. Dr. Kaneshige completed his Clinical Cardiology Fellowship at Creighton, where he also served as Chief Cardiology Fellow for two years. He completed an additional Cardiac Ultrasound Fellowship at the Mayo Clinic in Rochester, MN. Dr. Kaneshige served as Assistant Professor of Medicine at Creighton University School of Medicine, where he was Director of the Noninvasive Cardiovascular Imaging and Hemodynamic Laboratory.

Board certified in Internal Medicine, Cardiovascular Disease and Adult and Transesophageal Echocardiography

Ernest Pickering, DO, FACOI

Dr. Pickering is a cardiology specialist trained in noninvasive and invasive cardiology with subspecialty expertise in cardiac catheterization and angioplasty. He is Chief of Cardiology at SouthCrest Hospital and past Chief of Cardiology at



Tulsa Regional Medical Center. He completed a Cardiovascular Disease Fellowship at Baylor College of Medicine in Houston, TX.



Dr. Pickering's Internal Medicine Residency was completed at Oklahoma Osteopathic Hospital in Tulsa. He received his medical degree from Philadelphia College of Osteopathic

Medicine and his Bachelor of Science degree from Shelton College, Ringwood, NJ.

Board certified in Internal Medicine and Cardiovascular Disease

Edward T. Martin, MS, MD, FACC, FACP, FAHA

Dr. Martin is a noninvasive cardiologist with subspecialty expertise in non-invasive imaging. He is Director of Cardiovascular Magnetic Resonance Imaging at Oklahoma Heart Institute, SouthCrest Hospital and Hillcrest Medical Center. Dr. Martin is

also Director of Nuclear Cardiology at SouthCrest Hospital. In addition, he is a Clinical Associate Professor of Medicine at the University of Oklahoma College of Medicine – Tulsa.

Dr. Martin has specialty training in Nuclear Medicine, as well as additional training dedicated to Cardiovascular Magnetic Resonance Imaging. He completed his Cardiology Fellowship at the University of Alabama. Dr. Martin's Internal Medicine Internship and Residency training were performed at Temple University Hospital in Philadelphia. He received his medical degree from the Medical College of Ohio. Dr. Martin completed his Master of Science degree in mechanical engineering at the University of Cincinnati and his Bachelor of Science degree in physics at Xavier University. Dr. Martin is a founding member of the Society of Cardiovascular Magnetic Resonance and is an editorial board member of the Journal of Cardiovascular Magnetic Resonance.

Board certified in Internal Medicine and Cardiovascular Disease

Roger D. Des Prez, MD, FACC

Dr. Des Prez is a noninvasive cardiologist with subspecialty expertise in echocardiography, nuclear cardiology and transesophageal echocardiography. He is Director of Echocardiography and Peripheral Vascular Ultrasound Imaging at SouthCrest Hospital. Dr. Des Prez received his medical degree and Bachelor of Arts degree from Vanderbilt

University. He completed his Residency in Internal Medicine and Pediatrics at University Hospital of Cleveland. Dr. Des Prez practiced for six years as an internist with the Indian Health Services in Gallup, NM. He returned to Vanderbilt University as a

member of the Internal Medicine Faculty, at which time he also completed his cardiology training. In addition to noninvasive cardiology, Dr. Des Prez is interested in outcomes research and computers in medicine.

Board certified in Internal Medicine, Cardiovascular Disease, Adult and Transesophageal Echocardiography, Critical Care and Pediatrics

Christian S. Hanson, DO, FACE

Dr. Hanson is a specialist in Endocrinology, Metabolism and Hypertension at Oklahoma Heart Institute

with expertise in diabetes, lipids and hypertension. He also serves as Clinical Associate Professor of Medicine in the College of Osteopathic Medicine – Oklahoma State

University. He completed a Fellowship in Endocrinology, Metabolism and Hypertension at the University of Oklahoma in Oklahoma City. Dr. Hanson's Internal Medicine Residency and Rotating Internship were completed at Tulsa Regional Medical Center. He received his medical degree from Oklahoma State University and his Bachelor of Science degree from Northeastern Oklahoma State University in Tahlequah.

Board certified in Internal Medicine, Endocrinology and Metabolic Diseases

Rebecca L. Smith, MD, FACC

Dr. Smith is a noninvasive cardiologist with subspecialty expertise in transesophageal echocardiography, intra-operative echocardiography, stress and pharmacological

echocardiography and contrast echocardiography. She completed an Advanced Cardiac Imaging Fellowship at the Cleveland Clinic Foundation and her Cardiology Fellowship at the University of

New Mexico Health Sciences Center,

Albuquerque, NM. Dr. Smith's Internal Medicine Internship and Residency training were performed at the University of Arizona Health Sciences Center in Tucson. She received her medical degree from the Medical College of Ohio. Dr. Smith completed her Bachelor of Science degree at Cleveland State University.

Board certified in Internal Medicine

Tobie L. Bresloff, MD

Dr. Bresloff is a specialist in Endocrinology, Metabolism and Hypertension, with expertise in diabetes, lipids, hypertension and thyroid diseases. She also serves as Assistant Professor in Clinical Medicine at the University of

Oklahoma College of Medicine - Tulsa. She completed an NIH Fellowship in Endocrinology and Metabolism at Vanderbilt University in Nashville, TN. Dr. Bresloff's Internal

Medicine Internship and Residency were completed at Sinai Hospital of Detroit, Detroit, MI. She received her medical degree from Wayne State University School of Medicine in Detroit and her Master of Science and Bachelor of Science degrees at the University of Michigan, Ann Arbor, MI.

David A. Sandler, MD, FACC

Dr. Sandler is a cardiologist with subspecialty expertise in electrophysiology. He completed his Cardiac Electrophysiology Fellowship and his Cardiovascular Medicine Fellowship at New York University Medical Center, New York, NY.

Dr. Sandler's Internal Medicine Internship and Residency were performed at Mount Sinai Medical Center, New York, NY. He earned his medical degree from Georgetown University School of Medicine in Washington, DC. Dr. Sandler received his Bachelor of Arts degree at the University of Pennsylvania in Philadelphia.

Board certified in Internal Medicine, Cardiovascular Disease and Cardiac Electrophysiology

Raj H. Chandwaney, MD, FACC, FSCAI

Dr. Chandwaney is an interventional cardiologist with expertise in cardiac catheterization, coronary angioplasty and related interventional procedures such as coronary stents, atherectomy, intravascular ultrasound and peripheral vascular interventional procedures.



He completed his Clinical Cardiology Fellowship at Northwestern University Medical School in Chicago, IL., where he also completed an Interventional Cardiology Fellowship. Dr. Chandwaney's Internal Medicine Internship and Residency were

performed at Baylor College of Medicine in Houston, TX. He received his medical degree from the University of Illinois at Chicago. Dr. Chandwaney completed his Master of Science degree at the University of Illinois at Urbana-Champaign, where he also received his Bachelor of Science degree.

Board certified in Internal Medicine, Cardiovascular Disease and Interventional Cardiology

D. Erik Aspenson, MD, FACE, FACP

Dr. Aspenson is a subspecialist in Endocrinology, Metabolism and Hypertension at Oklahoma Heart Institute, with expertise in diabetes, lipids, hypertension and thyroid diseases. He com-

pleted a fellowship in Endocrinology at Wilford Hall Medical Center, Lackland AFB, Texas. Dr. Aspenson's Internal Medicine Internship and Residency were completed at David Grant Medical

Center, Travis AFB, California where he served as Chief Resident. He received his medical degree from the University of Oklahoma and his Bachelor of Science degree at Oklahoma State University.

Board certified in Internal Medicine, Endocrinology and Metabolic Diseases

Frank J. Gaffney, MD, FACC

Dr. Gaffney is an invasive and noninvasive cardiologist with subspecialty expertise in transesophageal echocardiography.

He completed his Cardiovascular Medicine Fellowship at Scott & White Memorial Hospital in Temple, Texas. Dr. Gaffney completed his Internal Medicine Internship and Residency

at Brooke Army Medical Center in San Antonio. He then remained on staff at Scott & White Memorial Hospital for several years, before entering his Fellowship in Cardiovascular Medicine. Dr. Gaffney earned his medical degree from New York Medical College, Valhalla, New York, and



he received his Bachelor of Arts degree at Hofstra University in Hempstead, New York.

Board certified in Internal Medicine and Cardiovascular Disease

Michael J. Fogli, MD, FACC

Dr. Fogli is a subspecialist in magnetic resonance imaging, nuclear cardiology, echocardiography, stress echocardiography and transesophageal echocardiography. He completed a fellowship in Advanced Cardiac Imaging at the University of

Texas, Southwestern Medical Center in Dallas, TX. His Cardiology fellowship was also performed there, as were his Internal Medicine Internship and Residency. Dr. Fogli earned his medi-

cal degree at the University of California, San Francisco School of Medicine and his Bachelor of Arts degree at the University of California, Berkley.

Board Certified in Internal Medicine and Cardiovascular Disease

Eric G. Auerbach, MD, FACC

Dr. Auerbach is a subspecialist in magnetic resonance imaging, nuclear cardiology, echocardiography, stress echocardiography and transesophageal echocardiography. He completed his Cardiovascular

Magnetic Resonance Imaging fellowship at Oklahoma Heart Institute, Tulsa, OK. His Cardiology fellowship was performed at the University of Miami/Jackson Memorial Hospital in Miami,

FL. Dr. Auerbach's Internal Medicine Internship and residency were also completed at the University of Miami/Jackson Memorial Hospital in Miami. Prior to that, he performed a Surgery Internship at New York Hospital/Cornell Medical Center, New York, NY. Dr. Auerbach earned his medical degree at the University of Miami School of Medicine, Miami, Florida and his Bachelor of Arts degree at Princeton University, Princeton, New Jersey.

Board Certified in Internal Medicine and Cardiovascular Disease

Kelly Flesner-Gurley, MD

Dr. Flesner-Gurley is a subspecialist in Endocrinology, Metabolism and Hypertension at Oklahoma Heart Institute, with expertise in diabetes, lipids, hypertension and thyroid diseases. Prior to joining Oklahoma Heart, she was at St. John Medical Center in Tulsa. She completed her fellowship in Endocrinology at the



University of Texas at Galveston. Her Internal Medicine Internship and Residency were completed at the University of Texas in Houston, where she also received her medical degree. She earned her Bachelor of

Science degree at Texas A&M University in College Station, TX.

Board certified in Internal Medicine, Endocrinology and Metabolic Diseases

Kambeez Berenji, MD, FACC

Dr. Berenji specializes in interventional cardiology including cardiac catheterization, coronary angioplasty and related interventional procedures such as coronary stents, atherectomy, intravascular ultrasound and peripheral vascular interventional pro-

cedures. He completed an Interventional Cardiology Fellowship at St. Vincent Hospital/Indiana Heart Center in Indianapolis, Indiana, where he then completed additional training dedicated to peripheral vascular intervention. Dr. Berenji performed

his Clinical Cardiology Fellowship at the University of Texas Southwestern Medical Center in Dallas, Texas and at the University of Iowa Hospital and Clinics in Iowa City, Iowa. He received his medical degree from Tehran University of Medical Sciences and then completed his Internal Medicine Internship and Residency at Wayne State University/Detroit Medical Center in Detroit, Michigan.

Board certified in Internal Medicine and Cardiovascular Disease

Robert L. Smith, Jr., MD, M.Sc.

Dr. Smith specializes in interventional cardiology including cardiac catheterization, coronary angioplasty, and related interventional procedures such as coronary stents, atherectomy, intravascular ultrasound, and

peripheral vascular interventional procedures. He completed an Interventional Cardiology Fellowship at the University of Florida College of Medicine in Jacksonville, FL. Dr. Smith performed his

Clinical Cardiology Fellowship at Vanderbilt University of Medicine in Nashville, TN and Tulane University School of Medicine in New Orleans. He received his medical degree from the University of Oklahoma College of Medicine in Oklahoma City and then completed his Internal Medicine Internship and



Residency at Emory University School of Medicine in Atlanta, GA. Dr. Smith received his Bachelor of Science and Bachelor of Arts degrees at the University of Oklahoma in Norman, OK.

Board certified in Internal Medicine, Cardiovascular Disease, and Nuclear Cardiology

Craig S. Cameron, MD

Dr. Cameron is a cardiologist with subspecialty expertise in electrophysiology, including the implantation and management of cardiac pacemakers, defibrillators, and cardiac resynchronization devices, as well as catheter ablation. He com-



pleted his Cardiac Electrophysiology Fellowship and his Cardiovascular Disease Fellowship at Baylor University Medical Center in Dallas, TX. Dr. Cameron's Internship and Internal

Medicine Residency were performed at Baylor College of Medicine in Houston. He earned his medical degree from the University of Kansas School of Medicine in Kansas City, KS. Dr. Cameron received his Bachelor of Science degree at Pittsburg State University in Pittsburg, KS.

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Fax 918.599.7036

Arthur J. Gallagher

Risk Management Services, Inc.

Dick Bryce

Dick.Bryce@ajg.com

1300 South Main
Tulsa, OK 74119
918.764.1654
Cell 918.232.3056

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Highlights from the 18th Annual Oklahoma Heart Update in Cardiology Symposium

LATE BREAKING CLINICAL TRIALS

This year at the Oklahoma Heart 18th Annual Update in Cardiology Spring Symposium, the results of several late-breaking clinical trials were presented. The highlights of several of those trials will be presented below.

The first trial to be presented was the Courage Trial. More than 1 million percutaneous coronary interventional (PCI) procedures are performed in the United States annually, the majority of which are done electively in patients with stable coronary artery disease. Prior studies have shown that percutaneous coronary interventional procedures decrease the frequency of angina and improve short-term exercise performance. The authors' hypothesis was that percutaneous coronary interventional procedures plus optimal medical therapy would be superior to optimal medical therapy alone. The study was funded by both the United States Department of Veterans Affairs, as well as the Canadian Institute of Health Research. Funding was also pro-

vided by several pharmaceutical companies. Fifty hospitals enrolled 2,287 patients between June of 1999 and January of 2004. The primary outcome was death or non-fatal myocardial infarction. Patients were randomized to either percutaneous coronary interventional procedure plus optimal medical therapy versus optimal medical therapy alone. Intensive guideline driven medical therapy and lifestyle intervention was performed in both groups. It should be noted that optimal medical therapy for both groups included anti-platelet agents, including aspirin and clopidogrel, statins, blockers of the renin angiotensin system, beta blockers, calcium channel blockers, and nitrates. In addition, case management was provided for lifestyle modification, including smoking cessation, exercise programs, nutritional counseling, and weight control programs. Patients were excluded if their ejection fraction was less than 30 percent, or if they had uncontrolled unstable angina, or had a history of sustained or symptomatic ventricular tachycardia or severe heart failure. All analyses were performed according to the intention to treat method. During the five year period, 3,071 patients were felt to be eligible.

However, 784 (26 percent) did not give consent. 450 of these had their primary physician fail to give approval for the randomization. Of the 2,287 consented participants, 1,149 were included in the primary analysis in the percutaneous interventional group and 1,138 were included in the primary analysis for the medical therapy group.

It should be noted that the intensive medical therapy treatment program was very effective in both groups of patients. For example, at 60 months, the average systolic blood pressures were lowered to 122 to 124mmHg, and LDL-cholesterols averaged 71 for the percutaneous coronary intervention group and 72 for the optimal medical therapy group. This represents outstanding control of their risk factors.

At a mean of 4.6 years follow up, 21.1 percent of the percutaneous coronary intervention patients required an additional revascularization due to restenosis, as compared to 32 percent in the optimal medical therapy group. The median time for subsequent revascularization was 10 months for the PCI group and 10.8 months in the optimal medical therapy group. What this means is that one-third of the patients in the optimal medical



therapy group switched over to revascularization with a percutaneous coronary interventional procedure; since this is an intention to treat study, these patients counted as "successes" in the optimal medical therapy group, despite the fact they had received interventional therapy.

The primary outcome was survival free of death from any cause and myocardial infarction. Overall survival differences were not significant between the groups. It should be noted that freedom from angina during long-term follow up was significantly better for the percutaneous coronary interventional group as compared to the optimal medical therapy group. At three years, 72 percent of the patients were free from angina in the interventional group, as compared to 67 percent of the patients in the optimum medical therapy group. This is statistically significant. The authors' conclusion was that as an initial management strategy in patients with stable coronary artery disease, percutaneous coronary interventional procedures did not reduce the risk of death or MI when added to optimal medical therapy. Therefore, they felt that optimal medical therapy, including aggressive management of multiple treatment targets without initial PCI, can be implemented in the majority of patients with stable coronary artery disease.

This study has provoked much debate regarding the use of medical management versus percutaneous coronary interventional procedures in patients with stable coronary artery disease.

It is essential to analyze the many limitations of this study. It is important to realize that this was a very select population. All the patients had an angiogram before deciding on therapy. It took five years at 50 centers to enroll only 2,287 patients. This represents less than 10 percent of the patients with angiograms at these trial sites. These facts must bring into question whether there was a very large selection bias with a very select group of patients. In addition, all patients with ejection fractions of less than 30 percent were excluded and in 26 percent of the patients, they were

unable to obtain consent.

The limitations of this study also included the fact that there was a very large crossover rate. Final outcomes were analyzed by the intention to treat method. Therefore, the group that the patient was originally assigned became the treatment strategy that was given credit for the long-term success or failure. It should be noted that one-third of the patients in the medical therapy group crossed over to percutaneous coronary interventional procedure, with a mean time to cross over of just 11 months of therapy.

There is also a question of the applicability of this study to real world care. First, nurse case man-

tion, since they don't have access to case managers for all their patients. It is also interesting that the trend was for the intervention group to do better than the medical therapy group in the non-VA hospitals and non-Canadian hospitals. This raises the question as to whether there could be a difference in treatment provided by the VA and Canadian National Health Service hospitals versus private non-VA hospitals.

Finally, the primary end-point death and MI was not significantly different between the two groups. However, in patients receiving interventional procedures, the freedom from angina was significantly better for the PCI group than the intensive medical therapy group. This is a very important factor. When patients continue to have symptomatic angina, it can greatly affect the quality of their lives. Therefore, freedom from angina is a significant benefit, even if there was not a significant difference in mortality or actual MI rates.

It should be noted that the Courage Trial did not change the current guidelines for emergency catheterization and percutaneous coronary interventional procedures for acute coronary syndromes. Studies still demonstrate the superiority of catheterization and intervention for acute coronary syndromes. The significance of this trial is that it demonstrates that it is reasonable in very select patients with stable angina, who are willing to follow a very aggressive risk factor modification program to proceed with medical management. This study indicates that you don't necessarily have to rush into percutaneous coronary interventional procedures at the time of diagnostic catheterizations. Diagnostic catheterizations with subsequent percutaneous coronary interventions, if needed and/or desired by the patient, however, is still a reasonable option.

Two clinical trials addressed the issue of who should receive primary prevention therapy for cardiovascular disease.

The MEGA Trial was presented in 2006. This trial looked at the management of elevated cholesterol in the primary prevention group of

The primary outcome was survival free of death from any cause and myocardial infarction."

agers intensely managed each of these patients during the five year study period in order to achieve optimal medical therapy. Most physicians and patients don't have access to nurse case managers to intensely manage each of their patients. In addition, the study demonstrated better than expected success rates for hitting risk factor targets. The mean LDL cholesterol levels were in the low 70s, and the mean systolic blood pressures were in the 120s. This provides testimony as to the excellent case management that was performed for these patients. However, most physicians are unable to get such outstanding results for a large patient popula-

adult Japanese. In this trial, 8,214 Japanese patients felt to be at low risk for cardiovascular disease were randomized either to diet therapy or diet plus low dose pravastatin 10-20mg. per day. They were then followed for an average of 5.3 years. Because this was such a low risk population, it was expected that this study might not show any benefit. The primary end point for this study was the development of a fatal or non-fatal myocardial infarction and new onset angina requiring revascularization. To the surprise of many, there was a 33 percent reduction in the primary end point at five years. This means that only 119 patients would need to be treated to prevent one serious adverse event. The MEGA Trial raised an interesting question as to whether we should be concentrating on low risk individuals as well as high risk individuals for cholesterol lowering strategies. An editorial about the MEGA Trial highlighted the following points: Low risk is defined as a less than five percent risk of a cardiovascular event over a 10 year period. In the United States, there are 25 million adults over the age of 40 who are considered low risk. In light of the fact that there was a 33 percent risk reduction in serious cardiovascular events in the MEGA Trial, then using statins in such a low risk population in the USA would translate into 125,000 fewer serious cardiovascular events over 10 years of statin therapy. For any other disease, this might be called an epidemic that could be treated.

The METEOR Trial was presented this spring at the American College of Cardiology meetings. This trial also evaluated use of statin therapy in low risk individuals. The METEOR Trial looked at the effect of rosuvastatin on the progression of carotid intimal-medial thickness, which has been shown to be a predictive surrogate marker of atherosclerotic cardiovascular disease. The METEOR Trial demonstrated that in the placebo group there was measurable significant progression of the carotid intimal-medial thickness over the

24-month study period. The rosuvastatin treated group showed no significant progression and there was a trend towards regression. The author's conclusion was that in middle-aged adults with low cardiovascular risk and evidence of sub-clinical atherosclerosis, rosuvastatin treatment over a two year period resulted in slowing of the rate of progression of the maximum carotid intimal-medial thickness compared to placebo and a slowing of the rate of progression in every carotid segment analyzed compared to placebo. This study highlights the issue regarding the treatment of risk factors for coronary artery disease in low risk populations. It should be noted that although a smaller percentage of patients in the low risk group will go on to develop symptomatic cardiovascular events, the greatest total number of myocardial infarctions and strokes occur in patients who are in the low risk population. These studies raise the question as to whether the current prevention guidelines need to be expanded to include lower risk patients.

In regards to treating symptomatic coronary artery disease, the MERLIN TIMI-36 Trial results were presented. The MERLIN TIMI-36 Trial looked at the use of ranolazine in acute coronary syndromes. Ranolazine represents the first new class of drugs to be approved for the treatment of angina in quite some time. Ranolazine blocks the late sodium channels and therefore may decrease oxygen utilization in ischemic myocardial cells. Since it does block the late sodium channels, there was a question as to whether its ability to prolong the QT interval could lead to serious dysrhythmic events. The MERLIN-TIMI-36 Trial evaluated both the efficacy and safety of ranolazine. The study randomized 6,500 patients with an acute coronary syndrome. They were randomized to either ranolazine I.V. followed by oral therapy versus placebo. The primary end point for the study was cardiovascular death, myocardial infarction, or recurrent

ischemia. There was a trend towards a slightly lower incidence of the combined events over the study period in the ranolazine group, but the differences were not statistically significant. If one looked at the secondary end points, it was found that recurrent ischemia by itself was significantly reduced by 13 percent in the ranolazine treatment group. This did achieve statistical significance. This would be consistent with the fact that ranolazine has been shown to be effective in the treatment of angina. The ability to decrease the incidence

These studies raise the question as to whether the current prevention guidelines need to be expanded to include lower risk patients.

of anginal episodes was seen in all the major sub group analyses that were performed. The safety results were also very encouraging. There were less clinically significant dysrhythmias seen on Holter monitoring in the ranolazine group as compared to the placebo group. The MERLIN TIMI-36 Trial demonstrated that ranolazine did not appear to be beneficial in the treatment of acute coronary syndromes. However, its efficacy for the treatment of chronic angina was once again demonstrated and, more importantly, the safety of ranolazine was demonstrated.

Finally, in looking at acute decompensated heart failure, the results of the Fusion-II Trial were presented at the American College of Cardiology meeting in March of this year. Fusion-II looked at the benefit of serial infusions of nesiritide for the management of patients with advanced heart failure. Fusion-II was designed to randomize 900 patients with advanced heart rate to receive



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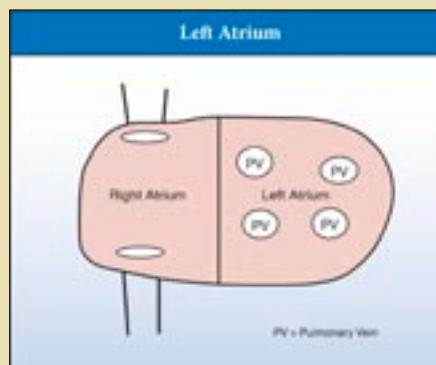
either nesiritide infusions two times a week versus placebo infusions two times a week, and nesiritide infusions once a week compared to placebo infusion once a week. The primary end point was time to all cause death or first cardiovascular and/or renal hospitalization through week 12. The study failed to show any difference in mortality, cardiovascular, or renal hospitalizations. All cause mortality was not significantly different between the groups. In this patient population with advanced heart failure, serial infusions of nesiritide showed no evidence of drug-induced renal harm, no evidence of increased mortality, but no clinical benefit. This once again raises the issue as to what the treatment options are for patients with severe but stable heart failure. We now know that patients who receive continuous intermittent infusions of inotropic agents, such as dobutamine or milrinone, clinically feel better, but have a higher long-term mortality rate. Unlike the studies using inotropic agents, nesiritide showed no adverse events with intermittent infusion therapy. However, in the absence of measurable benefit, it appears that the mainstay of treatment for patients with severe but stable chronic heart failure will include beta-blockers, blockers of the renin angiotensin system, spironolactone, hydralazine and nitrates, and aggressive use of diuretics.

Vasopressin antagonists may be the next class of drugs to be considered for management of chronic severe congestive heart failure. Recent trials do suggest benefit; however, more extensive trials will be necessary before the role of the vasopressin antagonist can be clarified.

Dr. Leimbach is a subspecialist in interventional cardiology, including cardiac catheterization, coronary angioplasty, and related interventional procedures such as stents, atherectomy, laser, intravascular ultrasound imaging, and direct PTCA for acute myocardial infarction.

Atrial fibrillation is a common arrhythmia affecting over 2.8 million Americans. Symptoms may include irregular palpitation, fatigue, and shortness of breath. Factors increasing the prevalence of atrial fibrillation include age, hypertension, obesity, and sleep apnea.

There are two strategies in dealing with atrial fibrillation. For some patients,



the best option is leaving them out of rhythm. The goals of management are to prevent stroke (by prescribing a blood thinner, usually warfarin) and controlling the heart rate. This is known as rate control. While this strategy may work well with elderly patients who are able to function well while in atrial fibrillation, others may require more aggressive control of their arrhythmia.

Rhythm control involves various measures to prevent future episodes of atrial fibrillation. Initially, anti-arrhythmic medications may be prescribed (see list of commonly used anti-arrhythmic medications). These drugs offer significant control of symptoms for many patients.

Commonly Prescribed Anti-Arrhythmic Medications	
Generic Name	Trade Name
Amiodarone	Pacerone, Cordarone
Dofetilide	Tikosyn
Flecainide	Tambocor
Propafenone	Rhythmol, Rhythmol SR
Sotalol	Betalapace, Betapace AF

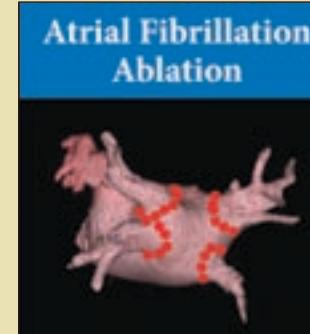
When symptoms are not controlled by anti-arrhythmic medications, catheter ablation may be considered. Ablation for atrial fibrillation is a procedure that eliminates the triggers of atrial fibrillation. In the 1990s, a group from Bordeaux,

France, discovered that the vast majority of triggers for atrial fibrillation arise within the four pulmonary veins. These are the veins which return oxygenated blood from the lungs to the left atrium.

Ablation therapy involves placement of multiple catheters (essentially insulated electrical wires) into the veins of the legs. These catheters are passed under X-ray into the heart. Once in the left atrium, the electrical connections between the pulmonary veins and the atrium are severed by placement of electrocautery lesions.

The success rate for this procedure is approximately 80 percent at one year. Like all cardiac procedures, atrial fibrillation ablation comes with some risk. Possible complications include stroke, vascular injury, and bleeding around the heart. Although these complications are rare (one percent), it is important to consider other options prior to proceeding with ablation.

As you can see, there is a wide spectrum of management options for patients with atrial fibrillation. While some patients may do well being left out of rhythm, some patients require aggressive procedures.



Dr. Sandler is a cardiologist with subspecialty expertise in electrophysiology, including the implantation and management of cardiac pacemakers, defibrillators, and cardiac resynchronization devices, as well as catheter ablation.



Eat Your Veggies!

A nutritional guide to produce

Everyone knows that eating a balance of fruits and vegetables daily is a healthful habit. However, not everyone recognizes the nutritional benefits brought about by specific types of produce. Some people may consider that putting a lettuce leaf and slice of

tomato on a sandwich suffices to balance a diet. However, this popular combination satisfies very few of your daily needs!

Packaged foods are required by the federal government to post a list of 'Nutrition Facts' — a guide which reveals the specific features

of the food you are eating: grams of protein, carbohydrates, and fat; milligrams of sodium, cholesterol, and potassium; and so forth. Alongside this information can be found the United States Food and Nutrition Board's (USFNB) recommended daily allowances (RDA) of each category broken down by percent. For conscientious eaters this information can be very helpful in planning healthful diets; for the rest of us, it is interesting, and important, to know what kind of stuff our consumables contain.

Unfortunately, when it comes to produce, such information is not so readily available. It's just too difficult to stamp each apple with the USFNB's RDA! We have all heard that an apple a day keeps the doctor away, but it's just as pertinent to know why!

Produce, like packaged goods, contains varying amounts of vitamins and minerals. Recognizing the kind that would be most healthful for you necessitates a bit of research to help you determine what you should be eating.

If you are one of the millions who wants to eat right, and have a good idea of why you are doing so, then the following guide is for you.

VITAMIN A

In plant form this vitamin is found as a carotenoid, recognizable as carotene, and is extremely valuable as a cancer preventer. The antioxidant qualities of carotene protect body cells from damage that can lead to cancer, making it a must-have on the menus of health-minded diners.

Vitamin A also contributes to the body's formation of epithelial tissue, a process which prevents the establishment and spread of infection. A diet complete with enough of this vitamin helps to keep the body's immune system healthy.

Typically, fruits and vegetables that are of deep hues — oranges, yellows, greens — have high carotene contents. Foods which contain 50% or more of the vitamin A RDA per serving include the following:

Apricots: the dried variety is also high in potassium.

Broccoli: vitamin C-rich, and high in calcium and potassium as well!

Cantaloupe: a densely nutritious vitamin C and potassium powerhouse!

Carrots: good source of potassium and soluble fiber.

Greens: also high in vitamin C and soluble fiber.

Mango: 130% of the RDA as well as all the vitamin C you need each day!

Papaya: features 300% RDA of vitamin C!

Sweet Potatoes: each cup contains 8 times the RDA!

Watermelon: contains significant amounts of vitamin C.

Winter Squash: strong vitamin C and fibrous content.

VITAMIN B COMPLEX

Vitamin B is the heading under which many different vitamins are classified. These B vitamins include thiamin (B1), riboflavin (B2), niacin (B3), folate, pyridoxine (B6), and cobalamin (B12). Working together, these vitamins contribute to the body metabolizing carbohydrate, fat, and protein. Without their presence in a diet, that otherwise healthy food you are eating could just turn to flab.

Most fruits and vegetables don't contain great levels of thiamin, riboflavin, or niacin, though this should not overly concern vegetarians; Americans are not at high-risk for deficiency diseases related to these three vitamins classified under the B banner.

Many fruits and vegetables do

contain significant amounts of folate, a nutrient essential for cell division and replication. This vitamin is, therefore, instrumental in healthy blood cell maintenance and production.

The items of produce which contain at least 25% of the folate RDA are as follows:

Beans: protein, potassium, fiber, and iron-rich, plus a veggie thiamin source!

Beets: a good source of starch and insoluble fiber.

Black-eyed Peas: a cooked cup also contains fiber, protein, potassium, and iron!

Broccoli: also contains high proportion of vitamin A, potassium, and calcium!

Cabbage: high in fiber and vitamin C as well.

Cauliflower: a comprehensive container of much vitamin C, potassium, and fiber!

Chick Peas: protein, fiber, iron, potassium, thiamin, and niacin all in one cooked cup!

Romaine Lettuce: the darker the lettuce color, the better!

Soybeans: calcium, potassium, iron, and protein add to this food's growing popularity!

Spinach: like other greens, a good source of vitamin C and fiber.

VITAMIN C

Perhaps the most recognizable and commonly found vitamin, this can be found in citrus fruits as well as many other fruits and vegetables. High levels are proven to be effective in fighting colds, and consideration of vitamin C as an anti-cancer agent is commonplace. This vitamin also contributes to the formation of cartilage, collagen, and bone, making it play a vital role in the diets of those recovering from accidents and elderly people.

The following foods are vitamin C-rich:

Asparagus: also a strong source of carotene.

Broccoli: along with vitamins A and B complex, this is high in calcium and potassium!

Brussels Sprouts: potassium, iron, carotene, riboflavin, iron, and a source of protein!

Cabbage: a source of fiber and vitamin B complex, too!

Cantaloupe: both vitamin A and potassium are here as well!

Cauliflower: a fibrous find for those seeking vitamin B complex and potassium!

Grapefruit: good source of pectin (insoluble fiber) as well as potassium.

Greens: the darker leaves are also a source for carotene and soluble fiber.

Honeydew Melon: also contains considerable potassium.

Mango: this fruit is a complete source for vitamin A as well as C!

Orange: a considerable source of folate.

Papaya: also high in vitamin A.

Plantain: good source of vitamin A, potassium, and fiber as well!

Strawberries: also contains pectin and potassium.

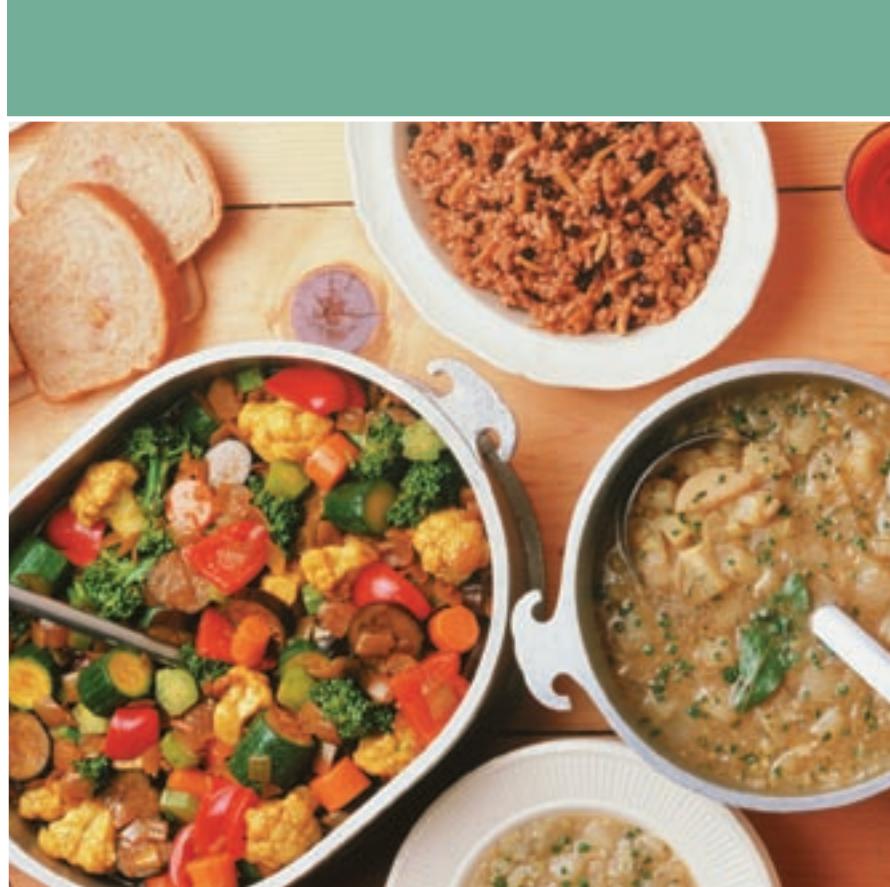
Sweet Potato: a great source of vitamin A!

Tangerines: a good source of vitamin A along with C.

Turnips: solid calcium and potassium content.

POTASSIUM

Potassium's purpose is multi-fold. Many people will be pleased to know it helps to check one's intake of sodium, keeping blood pressure down. It is important to maintain a balance between sodium and potassium in order to keep up a strong cardiovascular system. Potassium also serves the body in helping other foods accomplish nutritional purposes; without proper guides healthful foods can lose



their way, thereby losing their nutritional values!

A dietary allowance of approximately 3,500 milligrams is recommended by the FNB to maintain a healthy balance. The following foods contain at least 500 milligrams per serving:

Artichokes: mineral-rich, featuring calcium, iron, phosphorous and magnesium, too!

Bananas: you knew about the potassium, but do you know it is a soluble fiber source?

Black-eyed Peas: a storehouse of fiber, protein, iron, and vitamin B complex!

Cantaloupe: great source of vitamins A and C as well!

Dates: fiber-rich source of iron and B vitamins thiamin, riboflavin, and niacin!

Greens: look here for vitamin B complex and C as well as a good helping of fiber!

Beans: a high-fiber, iron-rich source of thiamin and protein, too!

Lentils: also a great (and relatively rare) vegetable protein source!

Parsnips: in addition features high levels of insoluble fiber.

Plantain: also contains vitamin A and fiber.

Potato: a good source of soluble fiber as well.

Rhubarb: also a decent source of vitamins A and C.

Soybeans: a high-protein comprehensive mineral source containing calcium and iron!

Tomatoes: vitamin A and C rich, these are considered a very healthful food!

Winter Squash: also a good source of vitamin C and fiber.

FIBER

Two types of distinct fibers can be found in many fruits and vegetables: insoluble and soluble. They serve distinct purposes and, though both are found in some produce, are generally taken in from different sources.



Insoluble fiber helps clear the digestive tract and is accordingly effective at preventing the development of cancer. Foods containing high levels of insoluble fiber, such as bran, are often considered to be ‘heavy’ foods: foods which fill a person up more than others despite having the same amount of calories

a feature which makes foods with high levels of this type of fiber excellent for those people watching their weight.

The following foods have high insoluble fiber content:

Beets: vitamin B complex and starch make this a very healthy food.

Berries: potassium and vitamin C can be found in the seeded varieties.

Grapefruit: also a potassium-rich food.

Parsnips: source of potassium.

Pears: four grams of insoluble fiber per: a high percentage!

Prunes: also contains soluble fiber, iron, potassium, and vitamin A!

Soluble fiber has a purpose with which many are not familiar — it bonds with cholesterol. This helps the body naturally dispose of the clogging characteristics associated with high-cholesterol levels.

Eating foods high in saturated fats and cholesterol contributes to a poor diet and should be avoided, particularly for those with high blood pressure. The following foods contain high levels of soluble fiber which can help assuage such problems:

Apples: also a good source of potassium.

Apricots: a vitamin A-rich food.

Bananas: a famous food for fulfilling potassium goals!

Beans: high levels of vitamin B complex, protein, potassium, and iron!

Black-eyed Peas: like other beans, has high mineral content as well as B complex!

Broccoli: what doesn't it have?! vitamins A, B, C, calcium, and potassium are here!

Cauliflower: contains potassium as well as vitamin B complex and C!

Corn: a good source of the minerals iron, zinc and potassium.

Eggplant: contains absolutely no cholesterol!

Figs: an excellent source of iron, calcium, and potassium!

Greens: a good source of vitamins A and C.

Lettuce: the darker the lettuce, the more vitamin A is present.

Okra: a decent source of vegetable protein.

Peas: vitamins A and C as well.

Potato: the potato's name shows it has a high potassium content!

Prunes: good food to enhance insoluble fiber, vitamin A, iron, and potassium intakes!

Zucchini: a moderate source of vitamins A, B complex, and C.

Many other important vitamins and minerals, such as vitamins E and K, calcium, iron, magnesium, and zinc, serve unique purposes and are present in the fruits and vegetables you eat; for more information, consult your doctor, nutritionist, or the numerous books on the market concerned with healthful eating.

Strict adherence to eating the foods listed here is not a necessity to living a healthy life; many people survive, and thrive, well enough without paying too much attention to what they consume. However, the more you know about what you are eating and what this does for your body, the more you will be able to control how well you feel. Ultimately, with a properly balanced diet featuring ample amounts of recommended and required nutrients, you can not only add years to your life, but can help yourself to feel better during that extra time!

DRUG ELUTING STENTS An Update

Percutaneous coronary intervention (PCI) has evolved as an important element of the standard of care in managing patients with coronary artery disease. Andreas Gruentzig performed the first successful human percutaneous transluminal coronary angioplasty (PTCA) on September 16, 1977.¹ Impressive acute and long-term success have been documented in that initial patient (see figure 1).² Unfortunately, despite the sustained benefit Andreas Gruentzig achieved in the initial patient treated with

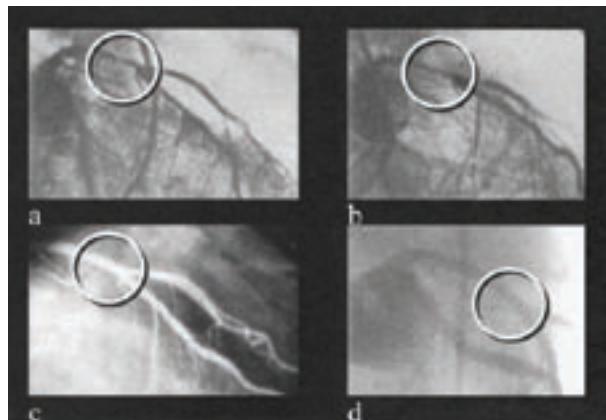


FIGURE 1 - Coronary angiograms of the first patient to undergo PTCA by Andreas Gruentzig. Panel A demonstrates the lesion before PTCA. Panel B demonstrates the lesion immediately post PTCA. Panels C and D demonstrate durable long-term outcome at the lesion site 10 and 23 years post PTCA, respectively.²

PTCA, such durable long-term outcomes could not be repeated reliably. Coronary restenosis became the Achilles heel of PCI (see figure 2).

The classically described pathophysiological mechanisms of coronary restenosis include elastic recoil, negative remodeling, and intimal hyperplasia. In fact, the processes that occur after vascular injury caused by PTCA are complex (see figure 3). These complex processes include mechanical stretch, endothelial denudation, vasoactive hormones, growth factors, circulating cells, lipids, extracellular matrix synthesis, and smooth muscle cell activation, migration, and oncogenesis.⁴

Coronary stents were the first arma-

ment that proved to be valuable in the battle against coronary restenosis. The European BENESTENT trial⁵, and its American equivalent STRESS trial⁶, were two landmark studies published in the same issue of the New England Journal of Medicine in 1994 documenting a significant reduction in coronary restenosis using the Palmaz-Schatz stent compared to PTCA alone. Since the publication of these trials, the worldwide use of coronary stents has grown exponentially. Coronary stents reduce restenosis by creating a scaffold to prevent elastic recoil and negative remodeling, thus eliminating two of the three classical pathophysiologic mechanisms of restenosis. Ironically, coronary stents cause the third mechanism of restenosis (intimal hyperplasia) to amplify (see figure 5). This concept has been well documented in numerous stent trials which demonstrate that late loss (a surrogate for intimal hyperplasia) is greater in coronary arteries treated with stenting rather than those treated with PTCA alone. Nevertheless, improved net gain is achieved, due to the greater acute gain that can be achieved with stenting (see figure 6).⁸ Despite improvements in bare metal stent technology, restenosis rates have continued to range from 25 to 35 percent.

Drug eluting stents are now recognized as the best weapon against coronary restenosis. After overcoming the obstacles of conducting a large amount of research with numerous drugs and polymer coating combinations, two drug eluting stent systems have been approved for clinical use.

The first drug eluting stent to be approved for clinical use was the Cypher sirolimus drug eluting stent manufactured by Cordis. Sirolimus is a natural

macrocyclic lactone, derived from the streptomyces fungus. It is a potent immunosuppressive agent developed by Wyeth-Ayerst Laboratories and approved by the Food and Drug Administration for the prophylaxis of renal transplant rejection in 1999. Sirolimus binds to an intracellular receptor protein and elevates p27 levels, which leads to the inhibition of cyclin/cyclin-dependent kinase complexes and, ultimately, induces cell-cycle arrest in the late G1 phase (see figure 7).⁹ The SIRIUS trial was the landmark multicenter, randomized trial that documented reductions in coronary restenosis with the use of the sirolimus eluting stent. Nine month in-segment restenosis was significantly reduced from 36.3 percent in the bare metal stent group to 8.9 percent in the sirolimus eluting stent group.¹¹

The second drug eluting stent system that was approved for clinical use was the Taxus paclitaxel drug eluting stent system manufactured by Boston Scientific. Paclitaxel is a naturally occurring compound derived from the Pacific yew tree with potent antiproliferative effects, thought to be due to inhibi-

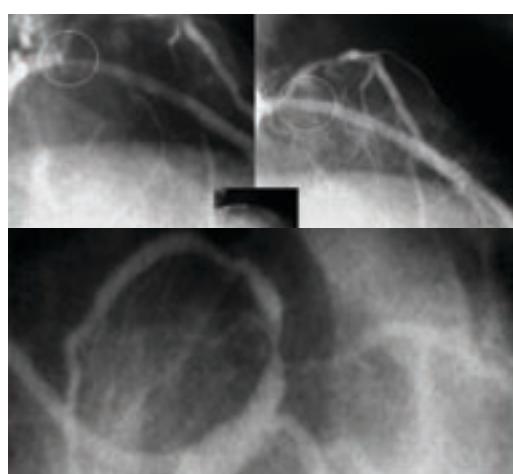


FIGURE 2 - Restenosis in PCI. Upper left image demonstrates severe stenosis pre PTCA. Upper right image demonstrates excellent result immediately post PTCA. Lower image demonstrates severe restenotic lesion 3 months post PTCA.³

tion of microtubule formation during the



mitotic phase of the cell cycle (see figure 7). The TAXUS IV multicenter, randomized trial

randomized trials of sirolimus eluting stents versus bare metal stents, and paclitaxel eluting stents versus bare metal stents, confirm the safety and efficacy of drug eluting stents.¹⁶

There is no statistically significant difference in mortality or myocardial infarction when drug eluting stents are compared to bare metal stents. The beneficial effect of drug eluting stents in reducing procedures for restenosis is still present at 4 year follow-up with both sirolimus and paclitaxel eluting stents (see figure 10). An interesting observation is the finding that although overall stent thrombosis rates are not different between drug eluting stents and bare metal stents, after 1 year thrombosis

elective surgery or major dental work in the next several months after stent placement would best be treated with a bare metal stent.

Several new drug eluting stents are undergoing clinical investigation and are expected to be approved for clinical use in the near future. Most noteworthy are the zotarolimus eluting stent by Medtronic, and the everoli-

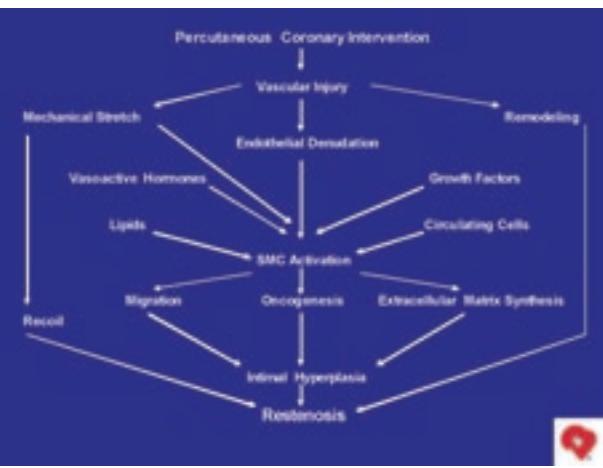


FIGURE 3 - Mechanisms of coronary restenosis.⁴

enrolled over 1300 patients and documented reductions in coronary restenosis with the use of the paclitaxel eluting stent. Nine month in-segment restenosis was significantly reduced from 26.6 percent in the bare metal stent group to 7.9 percent in the paclitaxel eluting stent group.¹²

In the fall of 2006, controversial research suggested a newly discovered problem of late stent thrombosis associated with the use of drug eluting stents. The BASKET-LATE study suggested increased rates of late stent thrombosis, non-fatal infarction, and death in patients who received drug eluting stents, compared to those who received bare metal stents (see figure 8).¹³ The absolute frequency of these events was noted to be low in both groups. Since the release of the BASKET-LATE study, both the FDA and the cardiology community have examined this issue very closely. A pooled analysis published in the New England Journal of Medicine, which included randomized clinical trials of sirolimus eluting stents reveals no significant difference in the rates of stent thrombosis between drug eluting stents and bare metal stents.¹⁴ This study utilized the standardized definition for stent thrombosis proposed by the Academic Research Consortium. A larger analysis of 14 trials and 4,958 patients evaluated the primary end-point of all-cause mortality during a mean follow-up 12.1 to 58.9 months.¹⁵ They found no difference in the incidence of death or the combined end point of death or infarction between sirolimus eluting stents and bare metal stents (see figure 9). Four year follow-up data of the

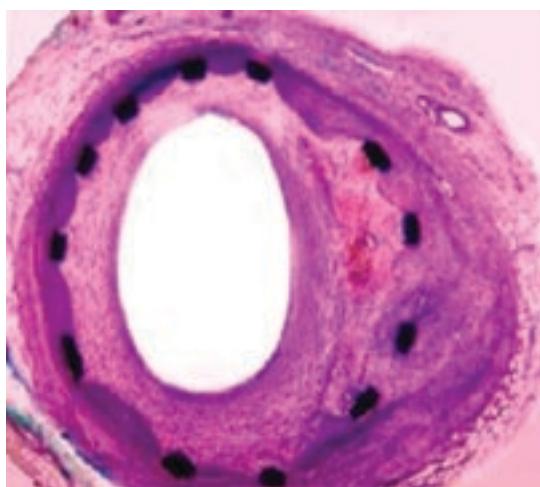


FIGURE 5 - Histological cross-sectional slide of a stented artery demonstrating adequately apposed stent struts with aggressive intimal hyperplasia causing restenosis.⁷

rates are more frequent with drug eluting stents.¹⁵⁻¹⁶

Most interventional cardiologists believe that drug eluting stents are beneficial in patients who can be expected to be compliant with an extended dual antiplatelet regimen. The American Heart Association and the American College of Cardiology advise that patients receiving drug eluting stents be treated with clopidogrel for 12 months, and aspirin indefinitely.¹⁷ Patients who are at a higher risk for bleeding complications, those unlikely to be compliant, and those who are expected to require

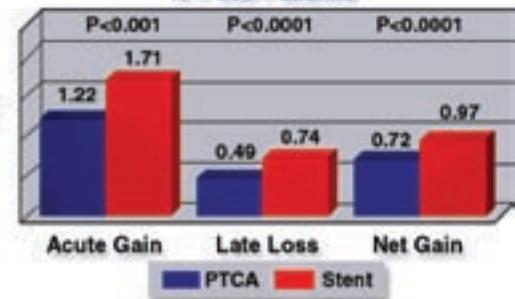


FIGURE 6 - Acute gain, late loss, and net gain in the STRESS I and II trials. This graph demonstrates that despite the increased intimal hyperplasia (late loss) observed with stenting, a net gain is achieved due to the greater acute gain that can be achieved at the time of the PCI.⁸

mus eluting stent by Abbott. Both of these drug eluting stents will be available on a more flexible (and hence more deliverable) cobalt-chromium platform. Both zotarolimus and everolimus disrupt the cell cycle at the G1 phase, similar to sirolimus (see figure 7). The ENDEAVOR III and IV trials suggest non-inferiority of the zotarolimus eluting stent in regards to target vessel revascularization, when compared to the sirolimus eluting and paclitaxel eluting stents, respectively.^{18, 19} Noteworthy, the zotarolimus eluting stent has been shown to have a small but significant increase in late loss when compared to the sirolimus eluting stent in

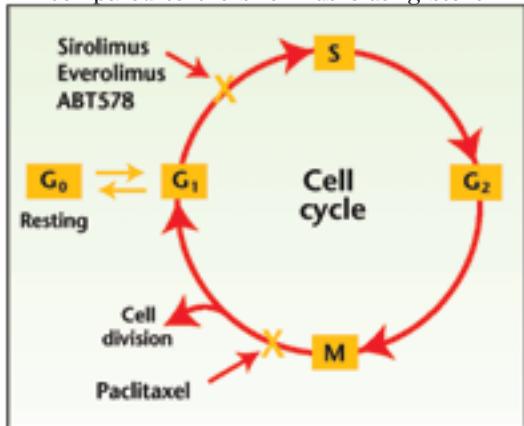


FIGURE 7 - Diagram of the cell cycle and locations that various drugs used in drug eluting stent systems have their inhibitory effects.¹⁰

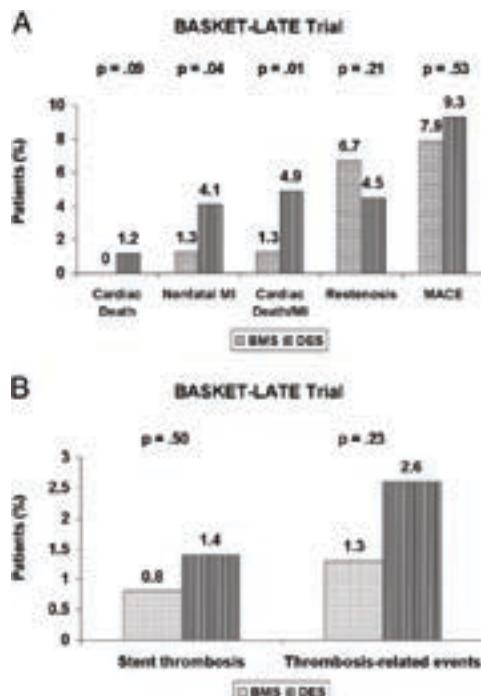


FIGURE 8 - Follow-up events occurring in the BASKET-LATE trial.¹³

the ENDEAVOR III trial. It has been hypothesized, but not yet proven, that this small increase in late loss may actually be protective from the perspective of late thrombosis. The SPIRIT III trial reveals non-inferiority of the everolimus eluting stent in regards to target vessel revascularization and superiority in regards to major adverse cardiac events, when compared to paclitaxel eluting stents.²⁰ The cardiology community eagerly awaits long term data examining the issue of late stent thrombosis and FDA approval of these advanced stent technologies.

The more durable results achieved with drug eluting stents have prompted investigators to wonder whether the outcomes achieved with multivessel PCI can rival those observed with coronary artery bypass graft surgery (CABG). The ARTS I trial compared the outcomes of multivessel stenting to CABG in the pre-drug eluting stent era. ARTS I showed no significant difference in mortality between the two groups, although there were a significantly greater number of repeat procedures required in the patients undergoing PCI due to restenosis.²¹ ARTS II compared a series of patients who underwent multivessel PCI with drug eluting stents to the historical CABG group in ARTS I. ARTS II revealed no significant difference in repeat procedures between the two groups and a trend toward a higher rate of major adverse cardiac events in the CABG group. These data are motivating

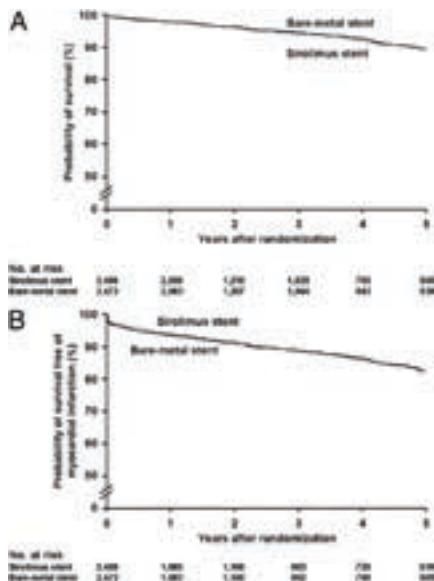


FIGURE 9- Effect of sirolimus eluting stent versus bare metal stent on subsequent death or survival free infarction.¹⁵

interventional cardiologists to recommend multivessel PCI with drug eluting stents, rather than CABG in patients who are appropriate candidates for either approach.²²

As of yet, limited data exist for the more challenging lesion subsets encountered in PCI. These challenging categories include unprotected left main disease, saphenous vein bypass grafts, bifurcation lesions, chronic total occlusions, restenotic lesions, and acute ST elevation myocardial infarctions. Small, and in some cases non-randomized, data collected in these types of patients are intriguing. Oklahoma Heart Institute plays an active role in this area by participating in multicenter trials designed to better understand how to best manage such complex patients. As drug eluting stent technology advances and the interventional cardiologist's experience with these difficult lesions broadens, we may be able to achieve a sustained, and universal, benefit in a broad variety of challenging lesions.

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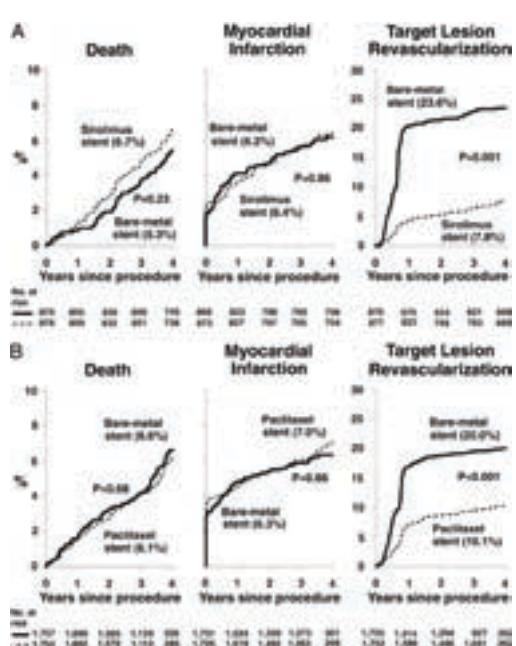


FIGURE 10- The 4 year follow-up of randomized trials of sirolimus eluting stent versus bare metal stent and paclitaxel eluting stent versus bare metal stent.¹⁶

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Dr. Chandwaney is an interventional cardiologist with expertise in cardiac catheterization, coronary angioplasty, and related interventional procedures such as coronary stents, atherectomy, intravascular ultrasound, and peripheral vascular interventional procedures.



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“They saved my life.”

At 62, Broken Arrow native Nick Aston was spending his retirement traveling the Pacific Northwest and Florida in his motor home. * It was on a visit home last February that he awoke with severe pressure in his chest. * He drove himself to Hillcrest Medical Center where a team of cardiologists was waiting to treat him. * Testing revealed he had three blocked arteries. Within hours a balloon angioplasty was performed and a stent inserted. * A few days later, Nick was released to Hillcrest's outpatient cardiac rehab program. * Today Nick is feeling better than ever and is once again ready to hit the road.



For a more in-depth look at all of our Stories from the Heart, call 585-8000 to receive your complimentary 32-page booklet.

Lake Claremore

*The
difference
is our doctors.*

 **Hillcrest**
Medical Center