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Fall 2013

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A
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TESTER,
TOO!



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* 35ng/mL

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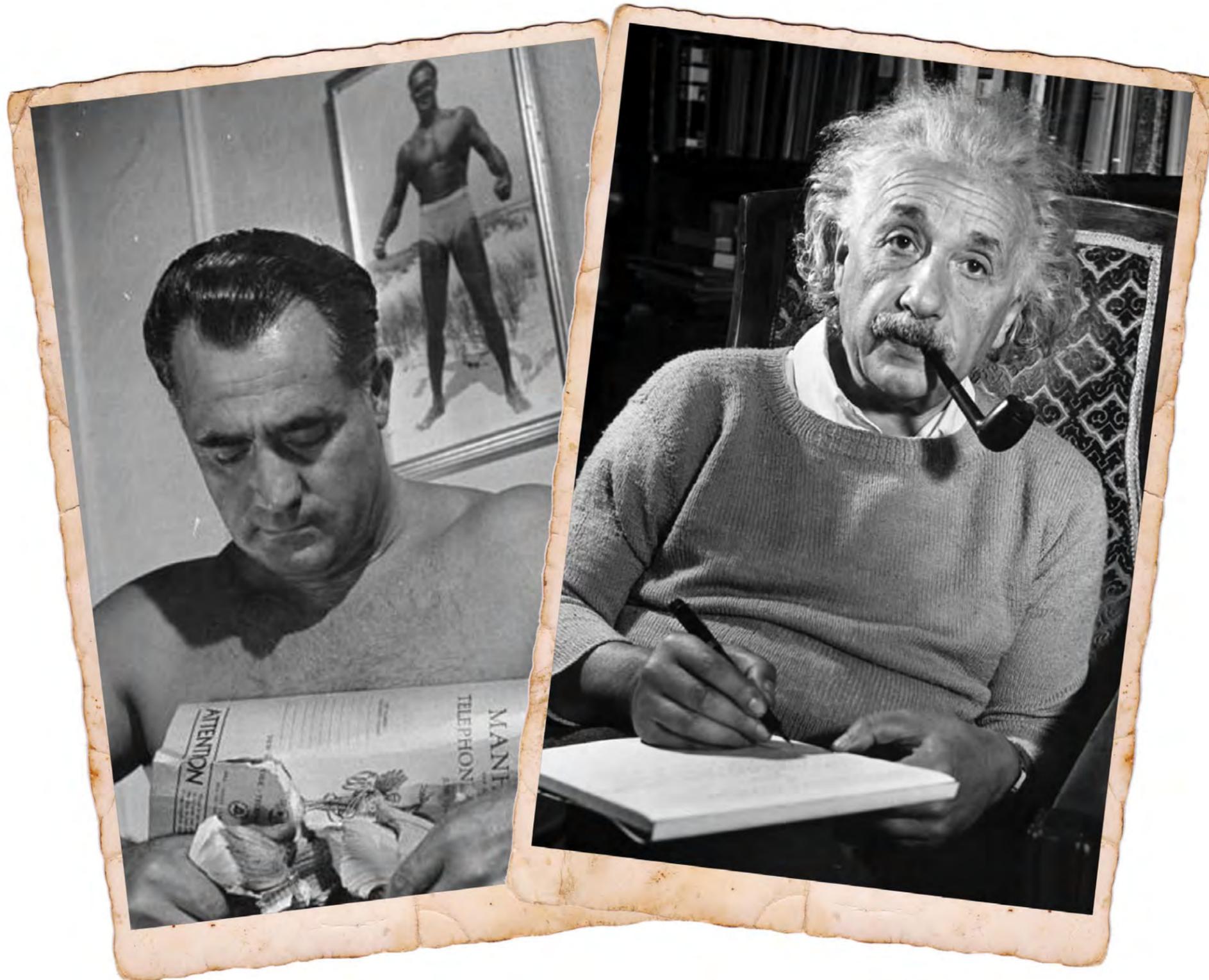
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PUTTING A NAME AND FACE TO HEART FAILURE



Rich, poor, black, white, man, woman, heart failure cuts a wide path across all strata of society. The famous are no exception. Here is a look at some renowned (and a few reviled) people who have died from heart failure¹.

BRAIN vs. BRAWN

Albert Einstein

Thanks to his theory of relativity, Albert Einstein became the most famous scientist of the 20th century. In 1905, while working in a Swiss patent office, Einstein published a paper proposing a "special theory of relativity," a groundbreaking notion that laid the foundation for much of modern physics theory. Einstein's work had a profound impact on everything from quantum theory to nuclear power and the atom bomb.

Albert Einstein was born at Ulm, in Württemberg, Germany, in 1879. In 1933, when the Nazis gained power, he renounced his citizenship and immigrated to America to take the position of Professor of Theoretical Physics at Princeton. In 1939, he sent a letter to President Franklin Roosevelt warning that Germany was developing an atomic bomb and urging Allied research toward the same goal. Einstein was famously rumpled with frizzy hair. His image has become synonymous with absent-minded genius. He died in 1955.

Charles Atlas

For much of the 20th century Charles Atlas (born Angelo Siciliano in 1892) was America's most famous muscle man. Atlas immigrated from Italy as a boy, and in his teens he built up his physique using a system of bodybuilding which he later dubbed "Dynamic Tension." His moniker

came from a friend, who after seeing a transformed Angelo declared, "You look like that statue of Atlas on top of the Atlas Hotel!" In 1928 the now Atlas met businessman Charles Roman and the two founded Charles Atlas, Ltd. and began selling bodybuilding courses by mail.

Atlas advertisements appeared in comic books and magazines and made Atlas into a pop culture icon; his most famous ad, a cartoon in which a scrawny young man resolves to bulk up after a bully kicks sand in his face, ran for years. (Atlas also popularized the phrase "97-pound weakling.") Atlas died at age 80 after a daily jog on the beach. He left behind a son, Hercules (and a daughter, Diana).

BLACK AND WHITE

George Wallace

The pugnacious spokesman for racial hatred, George Wallace stubbornly fought to preserve segregation in America, once even standing symbolically in the doorway of the University of Alabama to block two black students from enrolling. Wallace served four terms as governor of Alabama and ran for president of the United States four times. While on the campaign trail in 1972, Wallace was shot by a 21-year-old drifter named Arthur Bremer. He would spend his remaining years paralyzed, in a wheelchair.

After an unsuccessful fourth bid for the presidency in 1982, Wallace renounced his "Segregation now, segregation tomorrow, segregation forever!" stance and sought reconciliation with civil rights leaders. He was elected to the governorship, this time garnering substantial support

from black voters. Wallace died in 1998. One of those who came to pay their respects to the former governor was James Hood, one of the two students Wallace tried to stop from enrolling at the University. "I think he made peace with God," Hood told a reporter.

Thurgood Marshall

Attorney Thurgood Marshall led the landmark 1954 civil rights case of *Brown v. Board of Education of Topeka*, in which the Supreme Court declared state laws establishing separate public schools for black and white students unconstitutional. The decision stated that, "separate educational facilities are inherently unequal." Thirteen years later Marshall, a descendant of slaves, would become the Court's first African-American justice.

Marshall served on the Supreme Court for the next 24 years, compiling a liberal record that included strong support for Constitutional protection of individual rights. In the 1972 case *Furman v. Georgia*, which led to a de facto moratorium on the death penalty, Marshall articulated his opinion that the death penalty was unconstitutional in all circumstances. Marshall died in 1993 at the age of 84. In the aftermath, an obituary read: "We make movies about Malcolm X, we get a holiday to

honor Dr. Martin Luther King, but every day we live with the legacy of Justice Thurgood Marshall."

COPS AND ROBBERS

Al Capone

Alphonse "Al" Capone was one of the most notorious gangsters in history. The Chicago-based crime boss got his start in New York, working as a bouncer. After he inadvertently insulted a woman while working the door at a Brooklyn nightclub, Capone was attacked by her brother, his face slashed three times – which led to his "Scarface" nickname. Capone moved to Chicago in 1919 and quickly moved up in the ranks of Johnny Torrio's gang. It was Capone's men who gunned down seven rivals in 1929 in the "St. Valentine's Day Massacre."

Arrested many times over the years, Al Capone was famously pursued by federal agent Eliot Ness. Unable to find evidence to put him away for bootlegging and other vice crimes, Capone was finally convicted on income tax charges and sent to federal prison in 1931. After serving eight years, he was released on good behavior (and because he'd been suffering from syphilis-related ailments). Capone retired to his estate in Florida and died in 1947.

Jack Lord

Jack Lord is best known as Steve McGarrett in the long-running TV show *Hawaii Five-O*. Born John Joseph Patrick Ryan, Lord spent his early years in Queens, New York, attended the United States Merchant Marine Academy (his father was a steamship executive), then went to New York University on a football scholarship. During World War II, Lord was with the U.S. Army Corps of Engineers, building bridges in Iran (Persia at the time). While making maritime training films after the war, he took to the idea of acting.

Lord's first commercial film role was in the 1949 film *The Red Menace*, an anti-Communist production. Lord played the character Felix Leiter in the first Bond film, *Dr. No*. In 1966, Gene Roddenberry offered Lord the role of Captain Kirk on *Star Trek*. Lord demanded 50 percent ownership of the show. The part went to William Shatner. Lord would star for twelve seasons on *Hawaii Five-O*. He died in Honolulu, Hawaii in 1998 at the age of 77. His legacy may be a simple phrase he used that became pop culture: "Book him, Danno!"

Heart failure is more malignant than cancer.

GOOD vs. EVIL

Harry S. Truman

Harry Truman was Vice President for a year when Roosevelt died suddenly in 1945. Only months later, President Truman made the decision to drop two atomic bombs on Japan, ending World War II. Truman had a no-nonsense Midwestern style (A plaque on his desk read, "The buck stops here"). Truman was re-elected in 1948 in a contest many expected him to lose to the Republican candidate, Governor Thomas Dewey of New York. (A famous photograph shows Truman holding up a premature edition of the *Chicago Tribune* with the headline "Dewey Defeats Truman.")

The Cold War began under Truman's watch. The "Truman Doctrine" committed the United States to a policy of supporting foes of Communism everywhere in the world. Truman's failure to lead the United States to victory in the Korean War led to a severe decline in support for his policies among the American people. After leaving office, Truman retired to Kansas where he died in 1972 at age 88.

Kim Il-sung

Kim Il-sung headed North Korea's government from 1948 until his death in 1994 at age 82. Kim gained fame as a guerilla fighter against the

Japanese in Manchuria during the 1930s. When the Korean peninsula was split into North and South Korea in 1948, Kim grabbed power in North Korea (officially the Democratic People's Republic of Korea) and held it for the next 46 years. His official position was head of the Korean Workers' Party, but in fact he held near-total control over the country. Before Kim's death in 1994, he arranged for power to pass to his son, Kim Jong-il, who died in 2011, and who, in turn, relinquished power to his son and current ruler, the 30-year old Kim Jong-un.

Currently 26 million people live in North Korea, effectively cut off from most of the world. Former prison inmates who managed to defect and escape from North Korea have given harrowing evidence of the public executions and torture that are daily occurrences within the Communist dictatorship's jails.

BIG AND SMALL

Andre the Giant

André René Roussimoff, best known as André the Giant, was a professional wrestler and actor. He stood 7'4" and weighed 500 pounds. Born in Grenoble, France in 1946, Andre's parents, Boris and Marian Roussimoff, and four siblings were

all of average size. Andre, however, suffered from acromegaly, also known as Giantism. By the time he was 17 he stood 6'7".

Andre was wrestling in Canada under the name, "Monster Roussimoff" when Vince McMahon, Sr. of the then WWF spotted him, changed his name and quickly made "Andre the Giant" one of the most recognizable names in wrestling. Andre's last television appearance was on a TBS wrestling event, when he handed his title over to Hulk Hogan. Sadly, the effects of acromegaly continued to wear down Andre's body. He died in a Paris, France hotel room in 1993.

Shamus Culhane

"Heigh-ho! Heigh-ho! It's home from work we go!" sang the seven dwarfs as they marched home after a hard day's dig in their diamond mine. That scene from Walt Disney's first feature-length cartoon, *Snow White and the Seven Dwarfs*, was animated by Shamus Culhane. The scene took Culhane and his assistants six months to complete. *Snow White* premiered in 1937 earning \$8 million during its initial release, the record for highest grossing sound film at the time. Over the next 76 years it would go on to be one of the top ten North American grossing films ever.

Culhane's career, which spanned more than six decades, began before movies could talk and was accelerated in the sound era by his talent for synchronizing facial movements with dialogue. Culhane died in 1996 at the age of 88.

26 million people in the world have heart failure.

1 in every 5 people over the age of 40 will develop heart failure in their lifetime.

Heart failure is the number one reason people aged 65 or older are hospitalized.

Over 5 million people will die from heart failure this year.

HOW THE CARDIAC BIOMARKER ST2 IS CHANGING THE WAY CLINICIANS CARE FOR THEIR HEART FAILURE PATIENTS



MOST ACCURATE PROGNOSTIC CARDIAC MARKER

ONE CUTPOINT MAKES DECISIONS EASY

NOT AFFECTED BY COMMON CONFOUNDERS

THE IDEAL SERIAL TESTING CARDIAC BIOMARKER

ST2 IS IN THE ACC/AHA GUIDELINES!

When the natriuretic peptide biomarkers BNP and NT-proBNP were first introduced into clinical use a dozen or so years ago, they quickly established themselves as the gold standard for assisting in the diagnosis of heart failure. Their clinical value in prognosing and helping select treatments for heart failure patients, has been a different story, however.

BNP and NT-proBNP have not seen that same kind of successful utilization. As proof, after 10 years in the ACC/AHA Guideline for Heart Failure Management, natriuretic peptide markers still only garner a “C,” the lowest classification, for the body of evidence supporting their prognosis recommendation.

By contrast, the cardiac biomarker ST2, which received FDA clearance only in December 2011, was included in the new 2013 ACC/AHA update to the Guideline, receiving an “A,” the highest classification for the body of evidence supporting its recommendation as, “not only predictive of hospitalization and death in patients with HF [heart failure] but also additive to natriuretic peptide levels in [its] prognostic value.”

“ST2 has the highest prognostic value of any commercially available cardiac marker in predicting patient outcomes, allowing for the identification of high-risk heart failure patients for hospitalization, re-hospitalization and mortality, versus those at lower risk.”

As nearly 100 peer-reviewed published studies on more than 50,000 patients have demonstrated, ST2 has the highest prognostic value of any commercially available cardiac marker in predicting patient outcomes, allowing for the identification of high-risk heart failure patients for hospitalization, re-hospitalization and mortality, versus those at lower risk.

What Makes ST2 Better

- Besides its superior prognostic power, ST2 has a single cutpoint, removing any guesswork. If your patient’s ST2 level is over 35¹, that’s a warning sign.
- ST2 levels change rapidly in response to changes in the patient’s condition—sometimes within hours—making it a great serial biomarker.
- ST2 is not adversely affected by confounding factors such as age, body mass index, or impaired renal function.

“Individuals with high ST2 concentrations and on low beta blocker doses were almost seven times as likely to experience a cardiovascular event and the least likely to survive.”

Here are just a few examples of ST2’s prognostic ability from recent studies²:

Using ST2 to Guide Treatment

The results of a recent study conducted through the Massachusetts General Hospital, “Circulating Concentrations of Soluble ST2 Identify Benefit of High Dose Beta Blocker in Chronic Heart Failure: Results from the ProBNP Outpatient Tailored Chronic Heart Failure Therapy (PROTECT) Study,” highlighted the cardiac biomarker ST2’s ability to identify those patients most likely to benefit from high-dose beta blockers and thus reduce risk from cardiovascular complications.

Subjects were followed for 10 months. Individuals with high ST2 concentrations and on low beta blocker doses were almost seven times as likely to experience a cardiovascular event and the least likely to survive, by comparison to those with low ST2 concentrations

and high beta blocker dosage. Furthermore, ST2 levels “predicted time-to-first cardiovascular event above and beyond NT-proBNP and baseline clinical characteristics.”

“ST2 holds the link in potentially improving outcomes for heart failure patients through its unique ability to identify those who can benefit most from high-dose beta blocker treatment,” states Dr. James Snider, President of Critical Diagnostics.

ST2 Helps Lower Readmission Rates

In a *Clinical Chemistry* article, “Are Biomarkers the Answer to the Heart Failure Readmissions Problem?,” ST2 was declared to be “the most potent predictor of rehospitalization of all biomarkers assessed.”

Moreover, the study out of the Mayo Clinic, from which the data was drawn, demonstrated that serial changes in ST2 were superior to both BNP and troponin – the two most often used cardiac biomarkers – in the prediction of adverse events in otherwise stable chronic heart failure patients.

The paper highlights two potential roles for biomarkers in a strategy to reduce hospital readmissions for heart failure patients. The first is to help doctors identify people at risk for readmission, and second, to monitor serial values in the outpatient setting to allow for early intervention aimed at reducing readmissions.

Of the expected 1.1 million patients hospitalized for heart failure in the U.S. each year, one in four will be readmitted within 30 days of discharge. With an average cost per patient for rehospitalization of \$22,700, and \$35,800 per patient death, this high incidence of rehospitalization and mortality has a powerful negative financial impact on hospitals and the healthcare system as a whole.

Effective last October, hospitals with rates of rehospitalization for heart failure, MI, and pneumonia significantly higher than a defined target will lose one percent of their Medicare reimbursement across the board, meaning all Medicare reimbursements, not just those for heart failure. Under the law, next year that loss in reimbursements doubles to two percent, and then jumps to three percent in 2015. For many hospitals this will mean lost Medicare reimbursements that could easily exceed \$1 million.

As the paper pointed out, the use of BNP was “no better than a flip of a coin” in predicting hospital readmissions, and therefore in helping address this healthcare dilemma. Furthermore, the wide biological variation of BNP, which is affected by such confounding factors as age, body mass index, renal failure, smoking and other comorbidities common to heart failure patients, means “marked changes are necessary with BNP measures to be sure they are not simply due to spontaneous variation.” ST2 levels, by comparison, are not adversely affected by the normal confounding factors.

The use of BNP was “no better than a flip of a coin.”

ST2 Identifies Subjects Prone To Hypertension

A study titled, “Soluble ST2 Predicts Elevated SBP in the Community” published in the *Journal of Hypertension* found that a cohort of otherwise healthy individuals – showing no clinical signs or symptoms – except for high levels of the biomarker ST2 in their blood, were almost twice as likely to develop hypertension in the future than those with low ST2 levels.

Study investigators evaluated 1,834

individuals from the Framingham Offspring Study Cohort to determine the predictive utility of ST2 for progression of hypertension. The participants were followed over a period of three years. The results illustrated that those subjects whose ST2 level was elevated had a significantly greater chance of becoming hypertensive.

The implications of this finding are enormous. With this knowledge in hand, one day physicians may be able to offer patients tailored treatment options as part of a preventative approach to medicine that could delay or even forestall the onset of hypertension entirely.

“Subjects whose ST2 level was elevated had a significantly greater chance of becoming hypertensive.”

“ST2 is emerging as an important mediator of ventricular remodeling, as well as a valuable prognostic marker in cardiovascular disease,” state the authors. “Our findings support a robust link between sST2 and multiple [blood pressure] measures.”

ST2 Predicts the Onset of Heart Failure Years in Advance

The results of a study published in *Circulation*, an American Heart Association journal, showed the power of ST2 to predict development of heart failure and other adverse outcomes in the general population.

The Framingham Heart Study Cohort evaluated over 3,400 individuals to determine the prognostic utility of ST2 individually, and when combined with other biomarkers, to predict heart failure and other adverse events in people who are not medically perceived to be at risk. The study participants were followed for an average of just over 11 years.

“ST2 . . . was included in the new 2013 ACC/AHA update to the Guidelines, receiving an “A,” the highest classification for the body of evidence supporting its recommendation as, “not only predictive of hospitalization and death in patients with HF [heart failure] but also additive to natriuretic peptide levels in [its] prognostic value.”

As the study authors note, “sST2 [soluble ST2] is an emerging biomarker that has been shown to predict adverse outcomes and death in individuals with established heart failure.” The inclusion of ST2, a unique marker for cardiac remodeling and fibrosis, makes this study “the first to examine the prognostic value of sST2 measurements in the general population, showing that higher levels of circulating sST2 (comparable to those found in hospitalized patients) can be detected in apparently healthy individuals and precede adverse outcomes.”

When ST2 was used individually in the study as a marker of risk in fully adjusted statistical models, subjects with elevated ST2 levels were at 45% and 32% greater risk respectively for heart failure or death. Comparing those results in the same study with another biomarker, galectin-3, ST2 had twice the predictive value for heart failure or death. Moreover, when galectin-3 values were adjusted for kidney function, the association with incident heart failure was not statistically relevant.

“[H]igher levels of circulating sST2³ (comparable to those found in hospitalized patients) can be detected in apparently healthy individuals and precede adverse outcomes.”

It was late last year that another study, this one conducted through the Mayo Clinic, once again proved the remarkable accuracy of ST2 in

predicting the risk of heart failure and mortality in the general population. The study of 1,831 healthy individuals from Olmsted County, Minnesota, who were followed for approximately a decade, showed that those with the highest ST2 concentrations were at the most risk of heart failure or death over this same period of time.

Using ST2 To Identify Heart Failure Patients For Exercise Therapy

Ambulatory heart failure patients with lower ST2 levels may derive benefit from exercise. In a paper recently published in *Circulation: Heart Failure*, researchers from Duke University describe study results demonstrating that levels of ST2 are linked to how much a patient may benefit from exercise.

Exercise is often recommended for heart failure patients to help improve cardiac function and lower risk of adverse outcomes or death, but it has never been clear which patients would benefit most from exercise. The study found that patients with lower ST2 levels may actually derive benefit from exercise.

“To our knowledge, this is the most robust test of a novel biomarker to date with regard to covariate adjustment in a large, multicenter, cohort of ambulatory heart failure patients.”

Researchers used data from the HF-ACTION study to examine more than 2,300 patients with chronic heart failure who had the ability to exercise and were receiving optimal heart failure treatment. A subset of 910 patients who had available baseline plasma samples were used to measure levels of ST2.

In multivariable models, ST2 remained a significant predictor of outcomes after adjustment for clinical variables and NTproBNP. There was a statistically significant

interaction between exercise training and the outcomes of all-cause and cardiovascular mortality, such that patients with lower ST2 levels were more likely to have a benefit with exercise training than patients with higher levels.

““Biomarkers like ST2 could give us an entirely new window to the heart, help us risk-stratify patients, and also identify the patients who are healthy enough to benefit from exercise.”

“This is a great example of translational bench-to bedside research,” said Tariq Ahmad, MD, MPH, who led the study. “ST2, and its role in the heart, was identified in a basic science lab, and now we can evaluate what it means in a large, well phenotyped heart failure patient population. ST2 is one of the exciting new emerging tools in heart failure. It may give us unique insights into the pathophysiology of heart failure, and provide independent prognostic information about patient outcomes.”

“We want to get to a place with heart failure where we have a better understanding of what is happening in the heart at a molecular level, and we want to be able to better identify the sickest patients who are at greatest risk for being hospitalized and would benefit most from intensive therapies,” said Dr. Ahmad. “Biomarkers like ST2 could give us an entirely new window to the heart, help us risk-stratify patients, and also identify the patients who are healthy enough to benefit from exercise.”

“In this analysis of the HF-ACTION study, ST2 was found to be a significant predictor of long term outcome even after a very comprehensive adjustment for other covariates,” notes G. Michael Felker, MD, MHS, Associate Professor of Medicine at Duke and one of the study investigators. “To our knowledge, this is the most robust

test of a novel biomarker to date with regard to covariate adjustment in a large, multicenter, cohort of ambulatory heart failure patients.”

ST2 Predicts Organ Rejection and Death in Heart Transplant Patients

The results of a Utah Transplantation Affiliated Hospitals Cardiac Transplant Program study involving the use of ST2 to monitor heart transplant patients for rejection, showed that subjects with the highest levels of ST2 had a more than three-fold increase in the risk for death than those with the lowest ST2 levels. Moreover, this risk was present early and sustained from the time of initial blood draw to many years forward. Currently, biopsy-driven diagnoses are used to predict transplant organ rejection, but this type of procedure is costly, involves risk, and offer little consideration of the underlying biological processes that predict the presence or severity of rejection and/or likelihood of adverse consequences.

“[S]ubjects with the highest levels of ST2 had a more than three-fold increase in the risk for death than those with the lowest ST2 levels.”

In the ST2 study (“Interleukin receptor family member ST2 concentrations in patients following heart transplantation”), a total of 241 transplant patients were followed for a period of just over 7 years, during which time there were 62 deaths, or some 25 percent. The prognostic ability of ST2 was examined for both rejection and death. ST2 concentrations were measured approximately a month after transplantation and found to be highly predictive of short-, intermediate-, and longer-term outcomes.

(Continued on Page 12)

WHAT EVERY WOMAN NEEDS TO KNOW ABOUT HEART DISEASE

- Heart disease affects some 43 million women in the U.S.
- Heart disease is the No. 1 killer of women.
- Heart disease causes 1 in 3 women's deaths.
- More women than men die of heart disease.
- Heart disease is more deadly than all forms of cancer.
- Ninety percent of women have one or more risk factors for developing heart disease.

If you have questions about your health and heart disease, you should consult your physician or healthcare professional.

THIS MESSAGE HAS BEEN BROUGHT TO YOU BY

**CRITICAL
DIAGNOSTICS**
MAKERS OF THE ST2 ASSAY



"A monitoring strategy for the rejection that directly relates to its underlying pathophysiology would be an attractive choice," note the study authors. "Biomarkers reflective of rejection are an option . . . a novel biomarker candidate worthy of consideration for this application is ST2."

ST2 Is An Ideal Serial Marker For Monitoring Patients

The performance of a biomarker for serial testing is dependent, in part, on both its analytical and biological variability in clinical use.

"ST2 was shown to have the lowest RCV of any cardiac biomarker available, making it ideally suited as a biomarker for serial testing."

Analytical variability refers to imprecision of results by the measurement technique, and biological variability reflects the interindividual and intraindividual variance, respectively, between a relevant population of subjects and within a subject over time. In other words, both the precision of the assay itself, as well as its variability based on variances in the subject, i.e., if the patient had a meal before testing, or testing was in the morning versus the afternoon, can affect test results. This is obviously important when monitoring patients by serial testing.

A biomarker's Reference Change Value (RCV) reflects both the analytical as well as biological variability of the marker, and represents the change needed to signal a clinically meaningful change in a patient's condition or disease state. Biomarkers with lower RCV values require less change, then, to be clinically meaningful. This is obviously a big advantage when serially monitoring patients to avoid hospital readmissions.

In a seminal study published this year by Alan H.B. Wu, Ph.D., Professor

of Laboratory Medicine at UCSF, and Chief of the Clinical Chemistry Laboratory at San Francisco General Hospital, ST2 was shown to have the lowest RCV of any cardiac biomarker available, making it ideally suited as a biomarker for serial testing.

The study produced the following RCVs for these cardiac biomarkers: BNP = 138%; NT-proBNP = 92%; Galectin-3 = 61%; and ST2 = 30%.

ST2 Bests Galectin-3

In a head-to-head comparison of ST2 vs. Galectin-3 for long-term risk stratification of patients with heart failure, ST2 was found to be far superior.

Spanish study investigators followed 876 heart failure patients over a 5-year period, comparing ST2 and galectin-3's ability to predict all-cause death and cardiovascular mortality over conventional clinical assessment, using 11 standard risk factors (age, sex, NYHA functional class, estimated glomerular filtration rate, left ventricular ejection fraction, diabetes mellitus, sodium, hemoglobin, ischemic etiology of HF, ACE inhibitor or ARB drug treatment, and beta-blocker treatment) plus NT-proBNP. In a rigorous multivariate analysis, only ST2 remained independently associated with all-cause mortality and cardiovascular mortality. Galectin-3 was only significant in univariate models and the incremental predictive contribution of galectin-3 to existing clinical risk factors was, as the study authors graciously pronounced, "trivial".

"The same study also showed that ST2 adds considerable prognostic value even when the commonly used biomarkers for heart failure patient care are also considered, NT-proBNP, as well as high-sensitive troponin, both traditionally considered the 'gold standards' of cardiac biomarkers."

The same study also showed that ST2 adds considerable prognostic

value even when the commonly used biomarkers for heart failure patient care are also considered, NT-proBNP, as well as high-sensitive troponin, both traditionally considered the "gold standards" of cardiac biomarkers.

"In all studied cohorts with or without additional biomarkers, including natriuretic peptides, ST2 unambiguously emerged as a cardinal HF risk stratifier . . . these main findings suggest that the pathways identified by ST2 profoundly affect risk stratification in the context of chronic HF . . . The incorporation of ST2 into clinical practice for the prediction of all-cause and cardiovascular mortality should be readily contemplated by the practicing clinician."

Note the study authors: "This study highlights the importance of assessing the true value of emerging cardiac fibrosis biomarkers above and beyond clinical risk factors and natriuretic peptides particularly in light of the newly obtained ST2 . . . ACC/AHA class II recommendation for determination of prognosis in chronic HF. ST2 significantly refined discrimination and reclassification analysis while galectin-3 had negligible effects on performance metrics in risk prediction models.

"In all studied cohorts with or without additional biomarkers, including natriuretic peptides, ST2 unambiguously emerged as a cardinal HF risk stratifier . . . these main findings suggest that the pathways identified by ST2 profoundly affect risk stratification in the context of chronic HF . . . The incorporation of ST2 into clinical practice for the prediction of all-cause and cardiovascular mortality should be readily contemplated by the practicing clinician."

PLEASE NOTE: ST2 has been FDA cleared for use in risk stratification of chronic heart failure patients.

To learn more about ST2, go to: www.criticaldiagnostics.com.

HOW MUCH OTHER CARDIOLOGISTS EARN



How much do your colleagues make? According to a 2013 American Medical Group Association financial survey, the highest annual salary received by cardiologists is about \$811,000, with the average reported salary for a cardiologist at about \$403,000 annually. A lot depends, of course, on different factors like years of experience, level of specialization, practice choice and geographic location.

The starting salary for a cardiologist ranges from between \$180,000 to \$250,000. Cardiologists with more than 5 years of experience receive salaries averaging from between \$300,000 - \$400,000.

The typical annual salary for a cardiologist who performs cardiac & thoracic surgery ranges from between \$360,000 to \$522,875, for an invasive cardiologist it ranges from about \$272,000 to \$402,000, while pediatric cardiologists earn from about \$189,000 to \$230,900.

The five top paying states for cardiologists include South Dakota, Minnesota, Indiana, Nevada, and New Hampshire.

How does all this compare with other professions?

The president of the United States makes \$400,000 a year, plus free room and board.

For the 2013-2014 season, the average NFL referee salary is \$173,000, practice squad players make a minimum of \$6,000 per week, or \$102,000 for the full season, and an NFL player with less than one accrued season on the active roster would earn a minimum salary of \$405,000. *Forbes* magazine lists New Orleans Saints' Drew Brees the NFL top earner with a \$40 million salary plus endorsements deals worth \$11 million.

According to a survey by the National Association for Law Placement, a first-year public defender earned a median wage of \$45,700 a year, while a first-year prosecuting attorney made \$50,000 a year.¹ According to a survey by Major, Lindsey & Africa, a national legal search consultant, female law partners earn an average of \$497,000, while male partners earn an average of \$734,000.

The average starting pay for pilots at the major airlines is \$36,283 a year - about double what rookie pilots at many regional airlines get paid. Experienced captains top out at average minimum salaries of \$165,278.

While big-name celebrities like Tom Hanks and Angelina Jolie can earn \$25 million a picture, an average working film actor can make from as low as \$5,000 to \$50,000 per film.

The median hourly wage for fast-food cooks and cashiers is \$8.94, according to the National Employment Law Project. Assuming a 40-hour week, that's \$18,595 a year.

MANAGEMENT OF CRITICALLY ILL NEONATES WITH HEART DISEASE A FEW MINUTES WITH DR. KEVIN MAHER



Congenital heart defects - which can range from mild to severe - are the most common type of birth defect, affecting nearly one in every 100 newborns¹. Each year approximately 40,000 babies are born in the United States with a congenital heart defect. Congenital heart defects are the leading cause of all infant deaths in North America.

The Sibley Heart Center has 19 locations across Georgia that specialize in caring for children born with congenital heart defects, and for those who develop heart problems later in their childhood or teen years—also known as acquired heart disease.

Dedicated pediatric cardiologists, cardiac intensivists, pediatric anesthesiologists, pediatric heart surgeons and staff work together to heal thousands of children with heart problems each year. The center has one of the highest volumes of pediatric heart surgeries in the country.

Dr. Kevin Maher is a Founding Member and Associate Director at the Center for Pediatric Nanomedicine, a Director of Pediatric Cardiac Nanomedicine, an Associate Director, Atlanta Pediatric Device Consortium, and an Associate Professor of Pediatrics at Emory University School of Medicine. He is also a practicing Pediatric Cardiologist at Sibley Heart Center Cardiology.

We visited Dr. Maher a few months ago and were inspired and quite moved by the work he and other members of The Sibley Heart Center were doing. We asked him to tell us about his life and his work.

"I grew up in the suburbs of Baltimore Maryland, the second of four kids. We had a big yard, loads of animals, and a wonderful life. My dad was a local pediatrician, and my mom a nurse. In high school,

"I originally wanted to be an airline pilot, and then a summer job in a hospital following my freshman year in college changed everything for me."

my physics teacher was outstanding and contributed to my developing a love of science. I originally wanted to be an airline pilot, and then a summer job in a hospital following my freshman year in college changed everything for me.

"I completed my undergraduate degree in biology at Virginia Tech and then went on to medical school at the University of Maryland.

During medical school I had a senior professor (who, 30 years prior, taught my Dad!) named Dr. Woodward. He was a brilliant, compassionate person, and really taught the 'art' of medicine, and what it means to be a physician.

"We are currently working on a nanomaterial for coating tubing used in cardiac bypass or extracorporeal support (ECMO) that will hopefully decrease the risks associated with these devices for the sickest of children."

"I first got involved in pediatric cardiac nanomedicine due to my frustration with how we treat children with heart failure; essentially there is no good treatment for pediatric heart failure. I Googled 'pediatric nanomedicine' and found nothing, the field did not exist. I approached a well-known adult nanomedicine engineer at Georgia Tech (Gang Bao) and asked him if he would be interested in developing 'pediatric nanomedicine' as a field of study. He was very enthusiastic and we put together a proposal to create a Pediatric Nanomedicine Center.

"Children's Healthcare of Atlanta was very generous and pioneering to fund this center, the first of its kind in the world. Currently, Gang Bao, Paul Spearman (pediatric infectious diseases) and I run this center. We have in excess of 20 pediatric nanomedicine projects underway thus far and believe that these efforts will be the beginning of great advances in pediatric medicine. We are currently working on a nanomaterial for coating tubing used in cardiac bypass or extracorporeal support (ECMO) that will hopefully decrease the risks associated with these devices for the sickest of children.

"I also love the clinical part of my

career – having the knowledge, experience and skills to help provide very good care for critically ill children is a great feeling.

Pediatric cardiac services at Children's Healthcare of Atlanta are provided by the Sibley Heart Center. "We are a group of 45 pediatric cardiologists, with academic appointments at Emory University School of Medicine. Children's in Atlanta is one of the largest pediatric healthcare providers in the country, and has a large, successful cardiac program. This program provides state of the art, high quality pediatric cardiac care and is an extremely stimulating, challenging and rewarding environment to work in. I joined the program nine years ago.

"We see about 40,000 children each year as outpatients at Sibley, admit 1,300 each year to the cardiac intensive care unit, and perform 1,200 cardiac catheterizations

"People often ask how I can work in such an emotionally difficult environment. The truth is that the cardiac ICU is a very enjoyable and personally rewarding place to work. Seeing critically ill children get better and leave the ICU is simply a great feeling."

each year. In addition, about 900 cardiac surgeries are performed per year. All pediatric cardiac services are provided, from complex catheterizations, cardiac surgery, ventricular assist devices, cardiac transplantation, electrophysiologic services, pulmonary hypertension, genetic counseling, aortopathy clinic, to numerous others.

"People often ask how I can work in such an emotionally difficult environment. The truth is that the cardiac ICU is a very enjoyable and

(Continued on page 20)



You don't need a crystal ball to see that ST2 is the most prognostic of all cardiac biomarkers. The clinical evidence proves it.

ST2 is included in the 2013 ACC/AHA Guideline For The Management of Heart Failure, which calls ST2 "not only predictive of hospitalization and death in patients with HF [heart failure] but also additive to natriuretic peptide levels in [its] prognostic value." And the guideline gives ST2 its highest classification ("A") for the body of evidence supporting its recommendation.

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FOOD FOR THOUGHT

Check Please!

According to a Centers for Disease Control survey, Americans are checking their cholesterol levels more than ever before, and as a result, the number of adults who say they have had high cholesterol at some point in their lives has actually gone up.

That may not be a bad thing, though, because as the 2012 survey suggests, as Americans learn the importance of checking their cholesterol, in the last decade the overall level of high cholesterol among adults over 20 has dropped from 18% to 13%.

Moo Is Less

People who consume more than three daily servings of milk, yogurt, or cheese had systolic blood pressure almost four points lower than those who ate only half a serving daily, according to a study sponsored by the National Institutes of Health National Heart, Lung and Blood Institute.

And in a meta-analysis of 17 prospective studies published in the *American Journal of Clinical Nutrition* in 2011, that included over 600,000 participants conducted to assess the associations between milk product consumption and cardiovascular disease, for each 200-mL serving of milk consumed, a decrease of 6% in the risk of cardiovascular disease was observed.

Salty Language

No more than 1,500 milligrams of sodium a day, or a little more than half a teaspoon of salt, was supposed to prevent heart attacks and strokes in people at risk. Now a controversial report from an expert committee commissioned by the Institute of Medicine at the behest of the Centers for Disease Control and Prevention, said there was no rationale for anyone to aim for sodium levels below 2,300 milligrams a day.

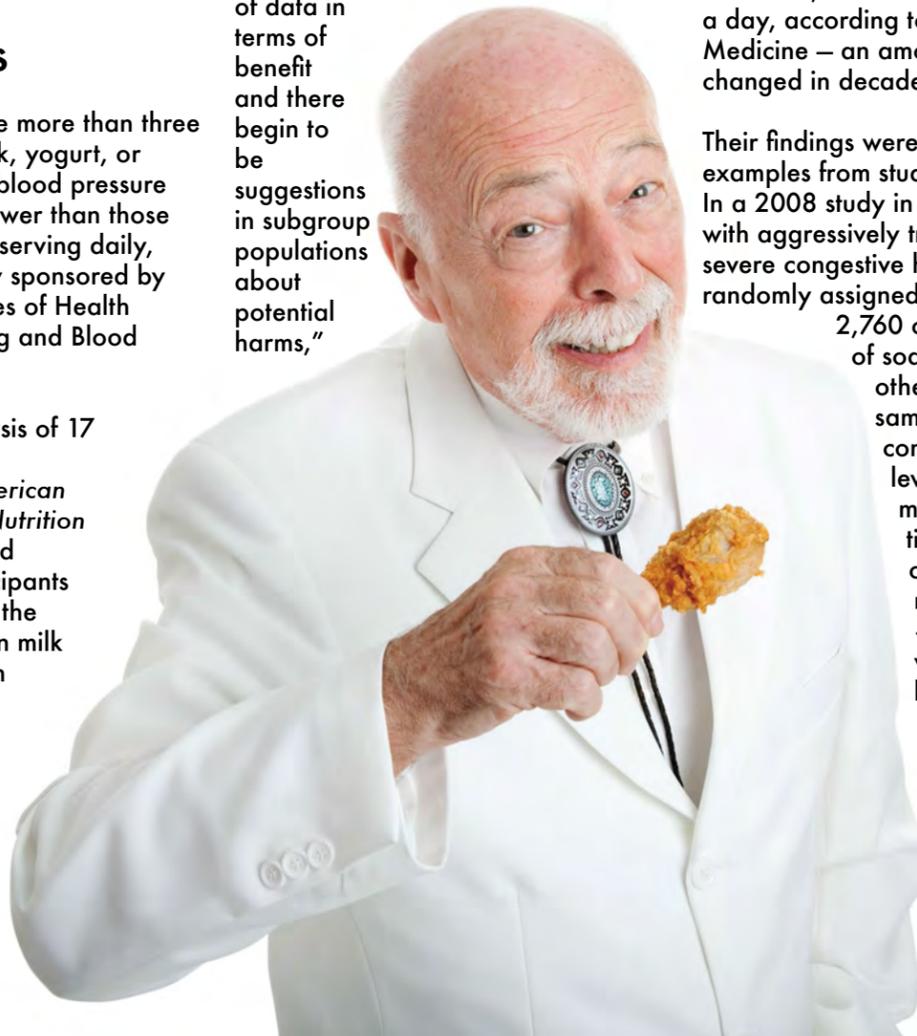
"As you go below the 2,300 mark, there is an absence of data in terms of benefit and there begin to be suggestions in subgroup populations about potential harms,"

said Dr. Brian L. Strom, chairman of the committee and a professor of public health at the University of Pennsylvania. He explained that the possible harms included increased rates of heart attacks and an increased risk of death.

The United States dietary guidelines, based on a 2005 Institute of Medicine report, recommend that the general population aim for sodium levels of 1,500 to 2,300 milligrams a day because those levels will not raise blood pressure. The average sodium consumption in the United States, and around the world, is about 3,400 milligrams a day, according to the Institute of Medicine – an amount that has not changed in decades.

Their findings were peppered with examples from studies they examined: In a 2008 study in Italy, 232 patients with aggressively treated moderate to severe congestive heart failure were randomly assigned to use either 2,760 or 1,840 milligrams of sodium a day, but otherwise to eat the same diet. Those consuming the lower level of sodium had more than three times the number of hospital readmissions – 30 as compared with 9 in the higher-salt group – and more than twice as many deaths – 15 as compared with 6 in the higher-salt group.

In another five-year study published in



2011, which followed 28,800 subjects with high blood pressure, ages 55 and older, the risks of heart attacks, strokes, congestive heart failure and death from heart disease increased significantly for those consuming more than 7,000 milligrams of sodium a day and for those consuming fewer than 3,000 milligrams of sodium a day.

"The American Heart Association is not changing its position," said a spokesman in response to the findings, rejecting the Institute of Medicine's conclusions, claiming the studies on which they were based had methodological flaws. The association's advice to consume 1,500 milligrams of sodium a day, the spokesperson added, is founded on epidemiological data and studies that assessed the effects of sodium consumption on blood pressure.

Whatever the truth is about the health effects of salt, it's clear it's likely to leave a bad taste in some peoples' mouths.

Don't Sugar Coat It

Salt isn't the only culprit when it comes to hypertension. Sugar, it turns out, is just as much of a silent killer. A 2008 study by the American Society of Clinical Nutrition found that excess consumption of fructose – a key ingredient in corn syrup used to sweeten many sodas – was linked to an increase in a condition called leptin resistance, a hormone that tells you when you've had enough food.

Drinking two-and-a-half or more cans of fructose-sweetened soda a day, or an equivalent amount of fructose from other foods, increases your risk of hypertension by at least 30 percent, the study found. What's more, the increased risk

appears to be independent of other dietary habits, including sodium, carbohydrate and overall calorie intake.



How Sweet It Isn't

Eating too much sugar can not only bring on hypertension, it can lead to heart failure, according to researchers at The University of Texas Health Science Center at Houston.

A study in the *Journal of the American Heart Association* showed strong evidence that sugar can actually affect the pumping mechanism of the heart and could increase the risk for heart failure.

The findings specifically pinpointed a molecule from sugar (as well as from

starch) called glucose 6-phosphate (G6P) that was responsible for the changes in the muscle protein of the heart. These changes could eventually lead to heart failure.

"When the heart muscle is already stressed from high blood pressure or other diseases, and then takes in too much glucose, it adds insult to injury," notes one of the study authors.

Super Sizing Your Risk

People who eat fast food four or more times a week increase their risk of dying from heart disease by 80 percent, according to a study published online in the journal *Circulation*.

Researchers analyzed the eating habits of 52,000 Chinese residents of Singapore who experienced a sudden transition from traditional foods to Western-style fast food, and then followed them over a 16-year period.

Other findings:

- People who consumed fast food even once a week increase their risk of dying from coronary heart disease by 20 percent, as compared to people who avoided fast food.
- The risk increased by 50 percent for people who ate fast food two to three times each week.
- Eating fast food two or more times a week increased the risk of developing type-2 diabetes by 27 percent.

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personally rewarding place to work. Seeing critically ill children get better and leave the ICU is simply a great feeling. There are times however when critically ill children do not survive their illness. We all find this extremely difficult, perhaps especially so when the children are older. It is very important to support each other and the families during these difficult times. A number of individuals and services at Children's are always available to help. It is part of doing this job, and we all lean on each other as needed.

"Not long ago I had a very complex patient with a single pumping chamber who was critically ill following surgery and did not look like he would survive. I thought that placing the child in a negative pressure chamber might improve his chances for survival. We tracked down one of these ventilators in Colorado and had it shipped overnight to Atlanta. The child made a dramatic recovery and was eventually discharged home and continues to thrive. His mother is aware of these efforts and whenever she and her son are at the hospital for outpatient visits they stop by the ICU to say hello."

"I see our field of pediatric cardiac

care becoming more collaborative, with research occurring at several centers simultaneously. Our patients will benefit from this shared knowledge and research findings. There is also a focus on quality and safety, especially in critical care. 'One is not zero' is a motto at Children's in Atlanta - aiming to have zero blood stream infections in the hospital.

"A number of people have impacted my life. For research and discovery, Dr. Mike Levine at the University of Maryland was a great mentor of mine. He started the Center for Vaccine Development and is a pioneer in this field. He is the greatest example I know of how drive and determination can result in accomplishing great things. For pediatric cardiac care, Dr. Peter Laussen (Sick Kid's Hospital, Toronto) and Dr. Anthony Chang (Children's Hospital Orange County) are both superb physicians, dedicated to advancing the science and practice of our field. They have served as mentors and have inspired me to push the envelope, and not accept the status quo.

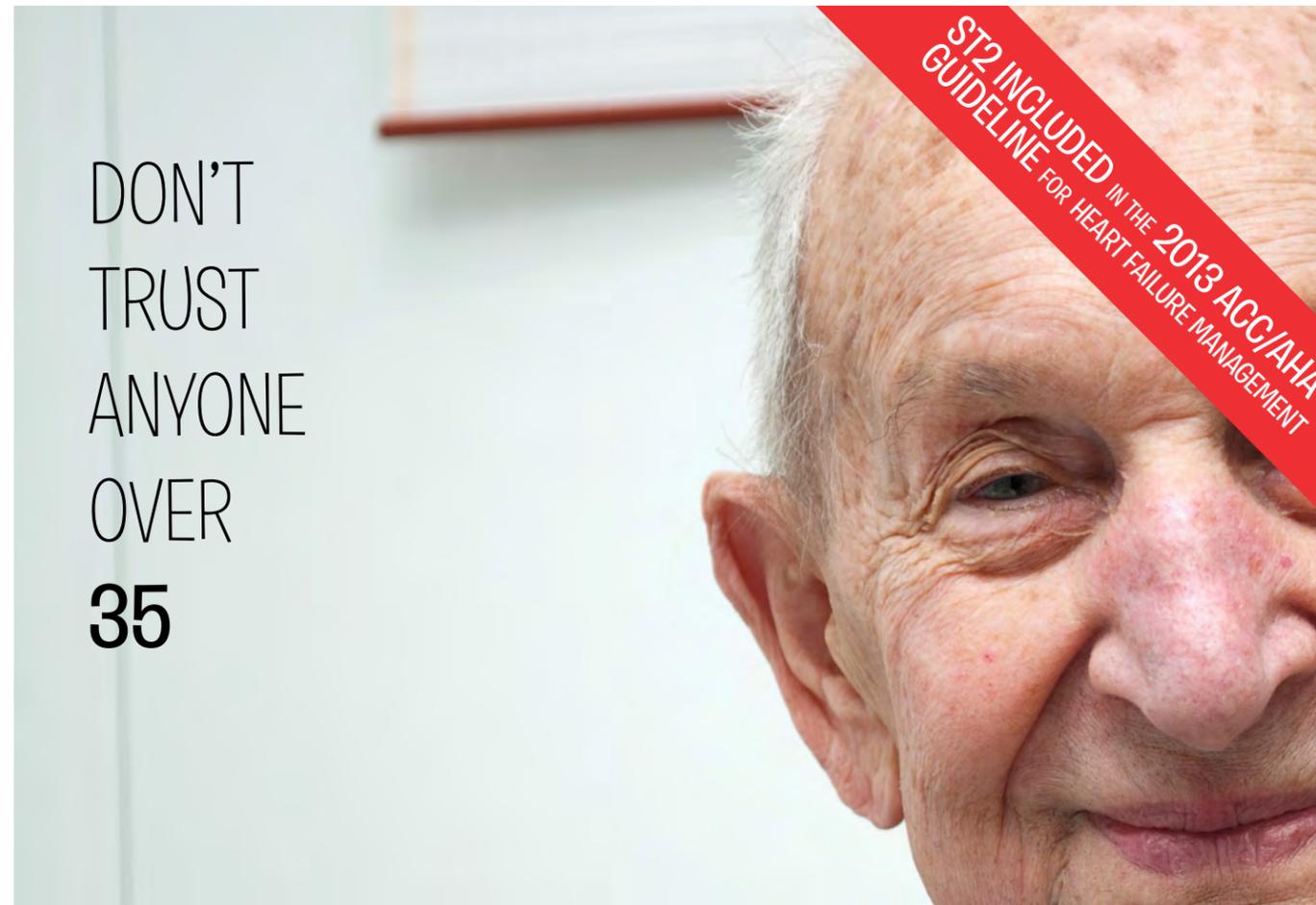
My 'hobbies' include watching soccer games and ultimate frisbee every weekend (we have three kids that

keep us busy). I often have building projects around the house, and have the kids help with these. Currently I am working on the kid's tree-house. I love to travel, and we do so whenever possible. We took our kids to Italy this past summer; it was simply a fantastic time.

"If a young cardiologist just starting out were to ask me for one piece of advise, I would tell that person to have passion, dedication and fun. It is an amazing, challenging and gratifying field of medicine. You can make a difference; go for it!"

"My favorite quote is by Mahatma Ghandi: 'Be the change you wish to see in the world.'

"If a young cardiologist just starting out were to ask me for one piece of advise, I would tell that person to have passion, dedication and fun. It is an amazing, challenging and gratifying field of medicine. You can make a difference; go for it!"



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ST2 is “not only predictive of hospitalization and death in patients with HF [heart failure] but also additive to natriuretic peptide levels in [its] prognostic value.”

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