breakthroug NUMBER 5 • SUMMER 2009

Ripple effect: Bayview is changing how caring clinicians are trained, and rewarded

Beating the Clock

C. the Difference!

"Good" Cholesterol, Infertility, and a Missing Gene

THE JOHNS HOPKINS CENTER FOR INNOVATIVE MEDICINE Medicine is a public trust



David B. Hellmann, MD., M.A.C.P. Aliki Perroti Professor of Medicine; Vice Dean, Johns Hopkins Bayview Medical Center; Chairman, Department of Medicine

FIVE SHORT YEARS

In this issue of *Breakthrough*, our two-part cover story reminds me of the classic TV commercial for Certs: "Two, two, two mints in one!" We don't have a secret ingredient (the Certs mints featured one called Retsyn). Instead, we have a powerful mission: To improve life for patients. The cover story features two programs – both the first of their kind – we have begun here at the Center for Innovative Medicine. *The Aliki Initiative* is designed to give the world more caring doctors; and *The Miller-Coulson Academy for Clinical Excellence* has been created to reward the excellent physicians we are blessed to have in academic medicine.

If you're not that familiar with the world of medicine, and particularly academic medicine, this work might seem like a no-brainer. Who doesn't want caring, clinically excellent physicians? In a perfect world, all patients would feel that their doctors knew them as people, cared about them, would go that extra mile to visit them at home and make follow-up calls just to see how they're doing. All academic faculty would be gifted clinicians, astute diagnosticians, and dedicated, inspiring teachers — and they would be rewarded for their excellence, just as scientific researchers are, with promotions and grants. In reality, it doesn't often happen this way. But we believe this should and can change.

I shouldn't be surprised, given the caliber of the people I work with here at the Center for Innovative Medicine, that we have accomplished so much in a very short time - but I marvel anyway at our progress. The CIM started just five years ago, with inspiration from Mrs. Anne Miller, and encouragement from Bill Brody, President of The Johns Hopkins University. If the CIM were – as I often think of it – a beloved child, we would be celebrating milestones like learning to ride a bike, and discovering letters and numbers. Instead, our five-year-old's accomplishments are helping to reshape academic medicine on many levels. As we told you about in our last issue, we have come up with a *new model for academic medicine* – a pyramid, with the patient at the pinnacle; teaching, research and patient care as each important corner; and at the base, the entire work force, all working together for the greater good of the patient. In addition to the Aliki Initiative and the Miller-Coulson Academy for Clinical Excellence, we have created key scientific and clinical research cores, which are engines driving scientific investigation and collaboration on this campus. Finally, at the CIM we have pulled together a bunch of bright, talented people, with whom I enjoy working immensely. Inspiration comes from all of these - the people, the programs, the creative thinking happening at every level, and above all, the patients. Recently, David Wessel, the Economics Editor of the Wall Street Journal, delivered our Sixth Annual Miller Lecture. As I listened to his astute analysis of medical care reform, it struck me that this lecture has become a major event at Johns Hopkins because we are hungry for such messages. The CIM is filling a powerful need. When we say that medicine is a public trust, we mean it, and we try to live it in everything that we do here.

David B. Hellown, M.D.

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WE BELIEVE

Medicine belongs to the public. Our mission is to create a different kind of academic medicine, to tear down ivory towers, share knowledge and dedicate ourselves toward one goal – making life better for patients.

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Ripple effect:

Bayview is changing how caring clinicians are trained, and rewarded

Why should it matter to a doctor where a patient keeps her medication? Maybe a better question is, why shouldn't this matter – especially when it might mean that a busy mom and caregiver might wind up back in the hospital?

Issues like these aren't in the medical books. But the stuff of real life – outside the hospital, when it's largely up to the patient and family to cope with an illness or try to recover from one – is as important, medically, as making the proper diagnosis and coming up with a treatment plan. What good is a treatment plan if the patient can't make it work?

Spreading the Word about Aliki

At Johns Hopkins Bayview, "old-fashioned" medicine – including house calls – has been given, medically speaking, a huge shot in the arm, with the help of the philanthropist, Mrs. Aliki Perroti. A groundbreaking educational program called "The Aliki Initiative," which started in 2007, has allowed residents and students to "get to know their patients more deeply, both inside and outside the hospital," says Roy Ziegelstein, M.D., executive Vice-Chairman of the Department of Medicine, and Co-Director of the Aliki Initiative. "The program reduces the residents' workload, and gives them more time to spend with their patients and teachers."

The word is spreading, most recently in Pharos, a journal for the medical honor society, Alpha Omega Alpha, that focuses on the humanities in the world of medicine. In a thoughtful article, Aliki physicians Neda Ratanawongsa, M.D., M.P.H., Ziegelstein, and others who have been involved with this exciting program lay out why what's happening here is so important. They also comment on the important role of philanthropy in helping to change medical education.

The busy mom and caregiver, called "Ms. P" in the article, is a case in point. A few days after Ms. P left the hospital, her Aliki Team intern and attending physician paid her a house call. They met her mother and son, and saw where all three kept their medications – in the same spot, on the dining table, where it might be easy to mix up or forget one or two pills among many

Once there was a doctor, a master diagnostician, known for his humanistic approach to medicine. A scholar, an expert in infectious diseases, the author of a classic textbook, called *The Effective Clinician: His Methods and Approaches to Diagnosis and Care.* This legendary physician and gifted teacher, named Philip Tumulty, was on the medical faculty at Johns Hopkins for nearly 50 years.

But the most remarkable thing about this man is that his patients just adored him. Tumulty was famous for his dedication to his patients. He spent hours with them, and if they were in the hospital, he was there, often well into the night. He cared, they knew it, and they cared back. When Tumulty died in 1989, many people believed his kind of medicine died a little, too – that "they don't make 'em like they used to."

Good news: They do! Even in a high-tech, reimbursement-driven medical climate that moves patients through clinics and hospitals quickly, these "old school" clinicians – some of them actually pretty young – gleam like diamonds. And a project begun at the Center for Innovative Medicine, with support from Anne Miller, one of Tumulty's former patients, and her daughter and son-in-law, Sarah Miller-Coulson and Frank Coulson, is aimed at recognizing, encouraging, and rewarding these outstanding clinicians – the "Dr. Tumultys" of today.

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The Miller-Coulson Academy of Clinical Excellence represents more than two years of painstaking work by the four Miller-Coulson Scholars, excellent clinicians themselves - Colleen Christmas, Chris Durso, Steve Kravet, and Scott Wright. They laid its foundation by defining academic clinical excellence – through many meetings with physicians and medical leaders at institutions across the country; empiric research studies, and an exhaustive review of the medical literature. Then, once they had defined something whose interpretation tends to be slippery – like great art, most people "know it when they see it" - they developed the clinical portfolio, a specific tool to measure the academic clinician's performance and contributions. They established an **External Review Board, identified potential Academy** members, and now, have elected their first six.

They are:

Nisha Chandra-Strobos, M.D., Professor of Medicine, Johns Hopkins University School of Medicine, and Chief of Cardiology, Johns Hopkins Bayview Medical Center, a compassionate clinician and perceptive teacher.

Michael Fingerhood, M.D., F.A.C.P., Associate Professor of Medicine, Johns Hopkins University School of Medicine, and one of the country's foremost experts on chemical dependency.

William B. Greenough III, M.D., Professor of Medicine, Johns Hopkins University School of Medicine, Professor of International Health, Johns Hopkins University Bloomberg School of Public Health, a pioneer in treating infectious diseases in the elderly, and in treating serious and complex wounds.

Jonathan E. Sevransky, M.D., M.H.S., Assistant
Professor of Medicine, Division of Pulmonary and
Critical Care Medicine, and Medical Director of
the Medical Intensive Care Unit at Johns Hopkins
Bayview Medical Center. Sevransky's clinical work
is dedicated to caring for the very sickest patients,
who need critical care.

Leah Wolfe, M.D., Assistant Professor, Johns Hopkins University School of Medicine, an excellent clinician and teacher in general internal medicine.

Roy Ziegelstein, M.D., Professor of Medicine, Johns Hopkins University School of Medicine, a gifted cardiologist and winner of multiple teaching awards. Ziegelstein is also Co-Director of the Aliki Initiative.

These six excellent clinicians were inducted during a special symposium in May. "It has been really exciting," says Christmas. "This was an opportunity not only to introduce our newly inducted members of the Academy to the public, but to tell the public about what we hope to achieve."

The first six Awardees are all from Hopkins. Next year, who knows? "Our greatest hope is that this is going to grow and spread like wildfire," Christmas says. "We have had incredibly enthusiastic responses from the External Review Board – that this is the right thing, that we need to do this all over the country. That's why we've gone about this in such a rigorous way, so that it can be reproduced at other institutions. The need for it is widely acknowledged."

"The best thing about this," adds Christmas, "is it reminds us that the qualities that make a great doctor like Philip Tumulty will never change."

A Blue-Ribbon Panel

"We looked around at the top departments of medicine in the country," says Colleen Christmas, M.D., one of the Miller-Coulson Scholars who helped select a half-dozen, nationally recognized medical leaders to make up the Academy's blue-ribbon advisory Board. This took many months, as the Scholars looked for leaders who would validate the seriousness of this effort. "We spent a lot of time thinking about, if we want to give this project credit, whom would everybody look to? Who would be in the best position to make a judgment?" says Christmas. "These are all extremely busy people. But luckily, everybody we asked was willing to do this. Everyone was very enthusiastic about the project."

External Review Board members include:

Holly J. Humphrey, MD

Professor of Medicine and Dean for Medical Education, University of Chicago Medical School

Lawrence S. Friedman, MD

Chair, Dept. of Medicine,
Newton-Wellesley Hospital
Assistant Chief of Medicine,
Massachusetts General Hospital
Professor of Medicine,
Harvard Medical School
Professor of Medicine,
Tufts University School of Medicine

David B. Reuben, MD

Archstone Foundation Professor of Medicine Chief, Geriatrics Division at the David Geffen School of Medicine, UCLA

Eric Holmboe, MD

Senior VP for Academic Affairs and Quality Research, American Board of Internal Medicine Professor Adjunct of Medicine, Yale University

Timothy Meagher, MD

Professor of Medicine,
Associate Executive Director of Medical
Affairs, McGill University Health Centre

Steven R. McGee, MD

Professor of Medicine,
University of Washington
Staff Physician, General Internal Medicine
Clinic, VA Puget Sound Health Care System
Division of General Internal Medicine

similar-looking jars. They brainstormed with Ms. P, coming up with ways to help her organize her medications, and to remember how to take them.

The Aliki physicians left Ms. P's home with a better understanding of the challenges of fitting a complex medical regimen into someone's daily life, and how to team up with the patient to find a solution that works. Ms. P appreciated that they took the time to come and see her. "I thought those days were over," she later told Ratanawongsa, "how the doctors used to come to your house. They sat down to talk...and that made me feel good... That's letting the patients know that someone else cares. That made me feel that I was important, and they're learning from me!" The most striking part of her Aliki experience, Ms. P recalled, was that "they treated me like I was the only patient they had to see that day. They treated me like I was someone special."

What good is a treatment plan if the patient can't make it work?

Although leaders of the Aliki Initiative hear and see for themselves, every day, how this program is helping young doctors and their patients, they are conducting numerous objective evaluations, as well. Some of these include:

- Looking for changes in Aliki residents' self-assessed behaviors, attitudes and skills before and after they take part in the program.
- Comparing the medical records of Aliki patients to those of other hospital inpatients, evaluating aspects of inpatient care, transitions of care, and the quality of discharge documentation.
- Examining the impact of the Aliki Initiative on patient outcomes, including hospital length of stay, quality and safety of the transition from hospital to home or another facility; rates of rehospitalization; patients' knowledge about their medical conditions and medications; and perspectives about the quality of their care and health care providers.

These and other studies, Aliki leaders believe, may help medical educators determine which aspects of this program should be implemented at other institutions, and may help secure grant funding to support such efforts.

None of this would have been possible without private philanthropy, notes Ziegelstein. "That an individual cares about the kind of doctors we are training reinforces the potential for medical education to flourish, when doctors and the public together view medicine as a public trust."

Ziegelstein recalls one of the most satisfying responses he has heard from an Aliki patient, to this question: "What could we have done differently during your hospitalization?" The answer: "You already did everything differently."

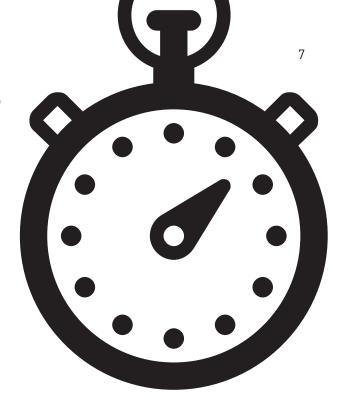
Beating the Clock:

When Time is Muscle

An artery shuts. The heart tissue it supplies – this can be an area very big, or very small – becomes ischemic. White, bloodless, aching, starving for oxygen, it starts to die very quickly, and the clock starts ticking.

When time is muscle, every little bit counts. A few minutes here and there can add up to a great difference – in saving a life, and in saving a heart. And this is what the Heart Attack Team at Bayview has done – shaved a whopping 20 to 30 minutes off of what cardiologists call "door-to-balloon time," the moment "the patient hits the door, to the time we inflate a balloon across the artery to open the blockage," says Jeffrey Trost, M.D., Co-Director of Interventional Cardiology.

Ideally, this period should take less than 90 minutes; state regulations require a door-to-balloon time of less than 120 minutes for 80 percent of all cases. This is sometimes easier said than done, especially in the wee hours of the night, or on weekends or holidays, when the hospital is not running at full staff - and when two-thirds of all heart attack patients come in. Until a couple of years ago, Bayview had room for improvement; then several things happened at about the same time. Innovations led by Eric Howell, M.D., (and reported on in our last issue, available on our website) sped up the flow of patients from the Emergency Department to the hospital. A groundbreaking triage program got patients admitted faster, cutting the average stay in the Emergency Department by 25 percent. Further improvements - which involved hospitalists thinking like air-traffic controllers, managing the flow of patients from Intensive Care to stepdown units made sure that ICU beds were almost always available. Because of this, Baltimore ambulances began bringing more heart attack patients to Bayview.



A few minutes here and there can add up to a great difference – in saving a life, and in saving a heart.

The next step was to get those patients to treatment even faster. Instead of waiting for the on-call balloon team to arrive, Trost devised a plan to use people who are already there – a critical care unit nurse, radiation technologist, and an emergency physician – to serve as a transition team, while the regular interventional cardiology team is en route.

"The transition team gets the patients upstairs, puts them on the table, attaches the EKG leads, administers medications if necessary, and does the preliminary preparation," says Trost. "Every step that the on-call team doesn't have to do is a minute saved." Even little things, like turning on the X-ray equipment, or putting a drape on the patient, add up.

The effort has paid off, in minutes. In 2008, the average door-to-balloon time was 79 minutes. "This is among the top 10 percent of any hospital in the country," says Trost. "And our outcomes are very good. It's one thing to do angioplasty quickly; you also have to help the patients do better. We are very proud of the fact that we have good door-to-balloon times, and our outcomes are terrific."

C. the Difference!

Proactive approach cuts hospitalacquired diarrhea rates by 40 percent

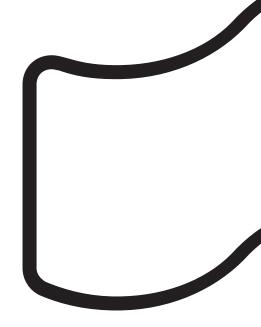
Clostridium difficile is in the category of nasty things that could be in our bodies – eyelash mites rank right up there – we would rather not think about. Fortunately, most of us don't have to think about this kind of bacteria, if all's well in our intestines.

Clostridium difficile ("c. diff." for short: difficile means "difficult" in French) is one of millions of different kinds of bacteria - good and bad - that live in the body. Most of the time, the "good" gut bacteria keep this difficult, rod-shaped, toxin-producing bacillus in check. But antibiotics - which kill helpful bacteria along with the bad bugs - can open a biological can of worms, create an imbalance in your intestines, and allow c. diff. to flourish. Unleashed, c.diff. wreaks intestinal havoc, releasing huge loads of toxins that cause inflammation, irritation and swelling in the colon, a condition known as colitis, with high fever, cramps, and diarrhea - lots of diarrhea. Rarely, this infection can lead to a hole, or perforation – a life-threatening condition that requires emergency surgery to remove part or all of the colon.

Technically, anyone who takes an antibiotic is at risk, but some are more vulnerable than others – particularly older people, seniors in nursing homes, and people who take antibiotics while they're hospitalized for another problem. At its very worst, c. difficile can be fatal; in fact, the death rate from c. difficile colitis more than quadrupled between 1999 and 2004. C. diff. is the major cause of hospitalacquired diarrhea in the United States and Europe.

Johns Hopkins Bayview is bucking this trend. In less than a year, a new, proactive approach among hospital patients has caused a 40-percent drop in new cases of c. diff. diarrhea, says Jonathan Zenilman, M.D., chief of Infectious Diseases, "It's a problem across the country," says Katie Passaretti, M.D., assistant professor of Infectious Diseases. Recognizing which patients are at greater risk, and then checking stool samples for any traces of this nasty bug, has made a huge difference. So has changing the way everybody involved - doctors in the hospital, community physicians, and patients themselves - thinks about antibiotics. Some basic rules are that less is more, and that narrowspectrum, more focused antibiotics are better than the superpowerful, broad-spectrum drugs (some of these include fluoroquinolones and Zosyn), which are often "overkill," says Passaretti. "We have put into place an antibiotic management program to

Less is more, and narrowspectrum, more focused antibiotics are better than the super-powerful, broadspectrum drugs, which are often "overkill."



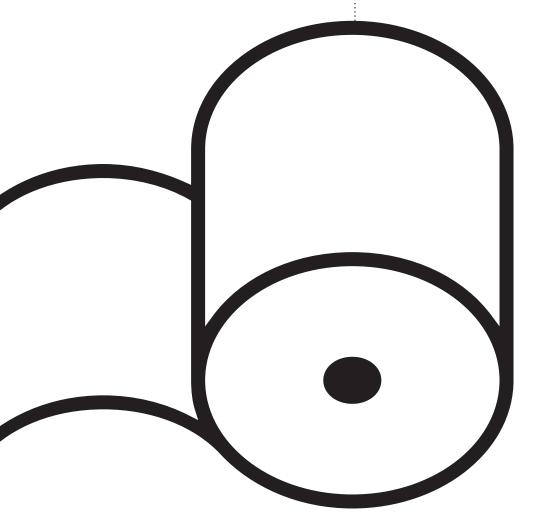
limit the use of certain super-powerful antibiotics," to review patient records and orders on medical charts, to make sure that if someone needs an antibiotic, it's an appropriate one. "If it's not, we communicate directly with the provider, to narrow down the antibiotic to one that is more focused."

One major benefit of these lower-caliber antibiotics is that they are much less expensive. As a result of the antibiotic management program's work, one expensive, high-powered antibiotic, once routinely stocked in the Emergency Department, has been replaced with an antibiotic that provides the same coverage, but at one-fourth of the cost, says Passaretti. Harder to calculate are the worst-case scenario cost savings of *c. diff.* colitis, which, if the patient requires surgery or intensive care, "can run into the tens of thousands."

It is an irony, says Infectious Diseases physician Katie Passaretti, M.D., that the fate of *c. diff.* is so entwined with antibiotics. The infection is caused by antibiotics, made worse by antibiotic resistance, and, most of the time, is cured with antibiotics. But it's becoming more difficult to treat – especially in people who have taken multiple antibiotics.

"It's a mindset," says Passaretti. "People think, 'I feel really bad. An antibiotic will make me feel better.' But really, you could be causing yourself more problems," and often, it's the passage of time, rather than antibiotics, that make the symptoms of a virus go away.

If you have a cold, do you need an antibiotic? "Only if you have a persistent high fever, or you're coughing up yellow or green stuff." If you're "just feeling crummy, with a runny nose, muscle aches, and clear phlegm," your best bet is to treat the symptoms individually, and save the antibiotics for when they can do the most good.



"Good" Cholesterol, Infertility,

and a Missing Gene

In a summer where the movie blockbuster is *Star Trek* – whose mission is to boldly go where no one has gone before – it is somehow fitting that Annabelle Rodriguez, M.D., is sailing into unchartered territory here at home, asking new questions, and making unexpected connections.

To understand her voyage, it may help if we make a brief side trip of our own, into the alphabet-soup world of blood cholesterol. Lipids are fat-soluble molecules. When a lipid joins a protein, it becomes a liproprotein; it also becomes a cholesterol-carrying vessel. the means of transport for cholesterol to move around in our blood. These lipidprotein combos are characterized by their density - high or low. HDL stands for "highdensity liproproteins," and the "H" here stands for happy, and heart-healthy, and other virtues. HDL is the "good" cholesterol - familiar to anyone who's ever had a blood cholesterol test, and been either praised for having a lot of the "good kind," or cautioned for having too much of the "bad kind," LDL. In contrast, having too much LDL (lowdensity liproproteins), suggests you're on the road to bad arteries.

At least, this is what doctors have believed for many years; but it probably is not that simple. Rodriguez is an endocrinologist, and Director of the Diabetes Management Service. She was intrigued by the discovery, made by Massachusetts Institute of Technology scientist Monty Krieger, of the HDL receptor. It is a scavenger receptor, known as SR-BI. In mouse studies, Krieger's group found that *not* having this receptor causes heart attacks, infertility in females, and early death. Most striking is that mice without this receptor have *high levels*

of HDL – so, in theory, all should be rosy and good in their arteries. But the high levels are artificial; the HDL is, basically, backed up in the bloodstream because it has no place else to go.

These findings struck Rodriguez, who has long been interested in the role of healthy cholesterol and how it protects against heart disease. The work in mice made her think of several patients she had seen, "with healthy cholesterol levels that were supposed to be in the desirable range, but who had a family history of heart disease, or who had heart disease themselves. I thought healthy cholesterol levels were supposed to protect you," she said. "Could this be the same in humans?" Rodriguez obtained an NIH grant five years ago to help her answer this question. Her results, published recently in the *Journal of Clinical Endocrinology and Metabolism*, show that people with low levels of SR-BI indeed have higher HDL levels,

and that certain variations within the SR-BI gene are linked to lower levels of the receptor.

Then Rodriguez went a step further – to the Hopkins infertility clinic. In 2007, Dr. Rodriguez showed that a sizeable number of infertile women undergoing *in vitro* fertilization had markedly lower levels of the receptor and lower levels of the female hormone

How does having less SR-B1 lower estrogen, and how does this affect progesterone, a key hormone required in pregnancy?

estrogen. This work was published in 2007 in Fertility & Sterility. Based on this novel observation, Dr. Rodriguez obtained support from a grant for translational research by Burroughs-Wellcome, and she is now taking blood samples from women with fertility problems to understand more specifically how this works. How does having a lower level of SR-BI lower estrogen, and particularly, how does it affect progesterone, a key hormone required in pregnancy?

"We hope to be able to come up with a diagnostic test in the very short term," says Rodriguez, "to help us define people who have a deficiency of this receptor." Because SR-BI is a scavenger receptor, it plays an important role in how the body repairs oxidative damage – countless tiny chinks in the DNA's armor, made every day by our food choices (particularly, by eating a lot of foods high in saturated fat), by smoking, drinking, or other environmental influences, as well as by genetic goings-on we can't yet explain. It may be that giving a cholesterol medication that also acts as an anti-oxidant will help restore fertility in these women.

This work, Rodriguez says, exemplifies "a lot of things that are fantastic about translational medicine. We have a conundrum in the clinic. We use information from different disciplines, from basic scientists, and geneticists, and it spawns off different approaches, so we're saying, 'I'm going to pursue this work from what you did.' and the response is, 'Wow! I never thought of it that way, but that's great!'" ■

Newsmakers

The Center for Innovative Medicine is blessed with excellent faculty – physicians and scientists who are excellent clinicians and also good teachers. It is always nice to see their work rewarded. Here are just a few recent examples:

Chris Durso, M.D., Associate Professor and Acting Director of the Division of Geriatrics, has received the *Dennis W. Jahnigen Memorial Award* from the American Geriatrics Society, for his nationally recognized and distinguished work in geriatrics education. (One of Durso's projects, the Miller-Coulson Academy, is featured on Page 5.)

Antony Rosen, M.D., has received the Mary Betty Stevens Award from the American College of Physicians (Maryland Chapter). This annual award is given to a physician leader who, in the tradition of the late Mary Betty Stevens, has made major contributions to our understanding of the pathogenesis and treatment of clinical disorders through human investigation. The award is fitting in many ways: Stevens was Chief of the Division of Rheumatology, a position now held by Rosen. And, Rosen is the Mary Betty Stevens Professor of Medicine. (Rosen's work with the CIM has appeared in previous issues of *Breakthrough*, available at our website: http:// www.hopkinsmedicine.org/innovative).

Eric Howell, M.D., Director of the Collaborative Inpatient Medical Service, has been promoted to Associate Professor of Medicine by the Advisory Board of the Medical Faculty. Howell and his talented colleagues – responsible for about 60 percent of all the patients admitted to the Department of Medicine – have used the inpatient service as a "laboratory" for studying and defining the most effective methods of providing inpatient care. His work has been published in the *Annals of Internal Medicine* and other publications, including *Breakthrough*. (Available online – see above.)

Steve Kravet, M.D., Assistant Professor in the Division of General Internal Medicine and President of Johns Hopkins Community Physicians, recently was given the Samuel Asper, M.D. Award for Clinical Excellence by the American College of Physicians (Maryland Chapter). The late Dr. Asper was Professor of Medicine at Johns Hopkins, served as Dean at the American University of Beirut, and as President of the American College of Physicians. His wide reputation as "the doctor's doctor" led the American College of Physicians to establish the award for clinical excellence in his name. (Kravet's work often appears in Breakthrough, including in this issue, on Page 5.).

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"There is a growing distrust of the value of academic medical centers. Some of this is deserved. We focus on publishing, rather than improving... on treating, rather than healing. We focus on spending, rather than innovating. The Millers recognized that this needed to change, and they created the Academy for Clinical Excellence."

From remarks made after the Sixth Annual Miller Lecture (see Page 2) by anesthesiologist and critical care physician Peter J. Pronovost, M.D., Ph.D., professor, Johns Hopkins University School of Medicine, Bloomberg School of Public Health, and Johns Hopkins School of Nursing, named one of the world's "most influential people" of 2008 by TIME magazine, for his work in patient safety.

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