

breakthrough

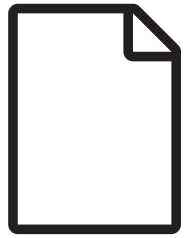
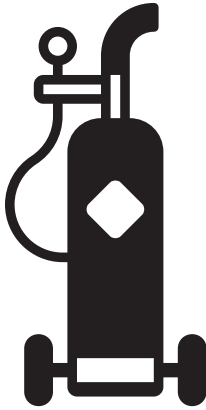
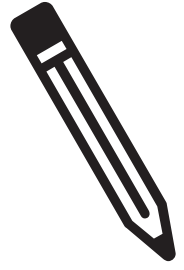
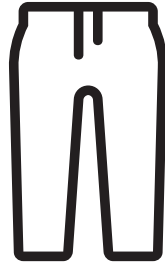
Thoughtful Little Changes

Quick-Changing Protein

What is Precision Medicine?

Golden Opportunity

How to Brew Good Ideas



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

breakthrough



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

SUMMER READING, WORK-LIFE BALANCE, AND WHAT ON EARTH IS PRECISION MEDICINE?

We read a lot around here. Every year, as we've reported previously in *Breakthrough*, our Advisory Board at the Center for Innovative Medicine has summer reading to do. We even have book reports. This summer, we read a book by Susan Wolf, a talented philosopher recently elected to the American Academy of Arts, entitled *Meaning in Life* and *Why It Matters*. Now, why would we read a book so far off the beaten path of medicine? Because good ideas can be found everywhere, and at a time when so many things are changing, I believe having focus on meaning in life is useful. I hoped that Wolf's book would give us an interesting context for examining the issues of work-life balance, and it did. Shortly after our discussions, a real-life issue of work-life balance occurred, and the result was that we were able to have John Burton – a legendary clinician who was considering retiring – start teaching our Chief Rounds (see Page 8). So now, while he has more time to spend with his family, our medical students, interns and residents have the golden opportunity to present patients to and learn from one of the most astute physicians in the world. It's a win-win.

I have enjoyed other reading, as well. Earlier this fall, the *New York Times* described our Aliko Initiative as an example of innovative design, where doctors in training "concentrate on a smaller number of patients. Though they work fewer hours, trainees now spend more time with patients, make house calls after people are discharged and learn outpatient care for chronic problems." And in completely different reading – of dozens of applications for our Pyramid Fund grants – I have been amazed and honored by the number of caring people we have here at Johns Hopkins Bayview who have suggested little ways that we can make a big difference to our patients (see Page 4). This fund gets its name from our Pyramid model of academic medicine, which places the patient at the very top; each side of the pyramid has scientists and clinicians involved in teaching, patient care and research, and where the sides meet are points of collaboration among doctors, nurses, scientists, therapists – the combinations are endless. The base is made up of all of the people who work here, who all feel that they are important to our mission.

In this issue of *Breakthrough*, you will see that very tiny things – such as a protein in the heart – can be of great importance, in a wonderful story of collaboration involving our Amos Proteomics Core and researchers in cardiology (see Page 6). You will also read about "Precision Medicine." What does that mean? It's a big idea, one we will be expanding on in future issues, but basically, many people can have the same illness, and yet some people sail through treatment with very few side effects, and some don't. Some develop complications involving other organ systems, and some don't, and of these, some with particular combinations do well with certain medicines, and others don't. It makes sense, then, that we must learn to sort out these various subsets of patients, so that we can do a better job of treating them. Antony Rosen (see page 10) is starting two pilot projects involving patients with rheumatic diseases that we hope will have applications throughout medicine.

Best wishes,

David B. Hellmann, M.D.

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Thoughtful Little Changes

Grants from the Pyramid Fund are deliberately small – some as little as \$50. But that's the point.

Golden Opportunity

A true giant in academic medicine is a treasure you do your best to keep.

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What is Precision Medicine?

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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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Thoughtful Little Changes

Eddie is on a ventilator. He's stuck there until he gets better; nothing much can change that at this point. But somebody – who watched him lying on his back all day, looking up at the boring fluorescent lights – wanted to help, and now, Eddie's world has changed remarkably. Because of something called a Skyscape, that white ceiling has become a lighted window to the outside world. Eddie can see clouds and trees. He feels calmer and, even better, more hopeful.

Eddie, and patients like him on the Plaza Unit in the Care Center, recently got their spirits lifted because Laura Doane, R.N., and her colleagues applied for a small grant from the Pyramid Fund. Recently in Breakthrough (for previous stories, see our website at www.hopkinsmedicine.org/innovative), we reported that this Fund was just being launched. The Pyramid, the brainchild of Vice Dean David Hellmann, M.D., is a new model for academic medicine in which the patient is at the very pinnacle; there is collaboration among teachers, clinicians, scientists, and nurses; and staff at every level are involved, and know that their ideas and contributions are important. Springing from this, the Pyramid Fund – open to all Johns Hopkins Bayview staff and faculty – is designed to support creative ideas, projects or innovations that can help brighten the day for patients and their families. As grants go, Pyramid project monies are deliberately small – ranging from as little as \$50 to \$1,500, with a total annual budget of \$25,000. But that's the point: The Fund encourages little ideas that have the potential to have a big impact.



"The enthusiasm for this blew me away," says Hellmann. Indeed, says Cindy Rand, Ph.D., Deputy Director of Patient-Centered Care, "we have clearly tapped into a tremendous desire of many people to make thoughtful changes to help our patients. There are a lot of people around here who really care."

This summer, a multidisciplinary review committee that included faculty, nurses, social workers and administrators received 40 proposals and funded 20 of them: 12 went to applicants in the Department of Medicine, three in Psychiatry, three in Pediatrics, one in Surgery, and one in the Harrison Library. Recipients included 11 nurses, four faculty, two dietitians, two members of the house staff (interns and residents), three patient care technicians, a social worker, a physician's assistant, a Child Life specialist, a librarian, a therapist, and a research assistant. The total cost of these 20 awards was less than \$13,000. "We were very impressed with the caliber and creativity of the applications," says Rand, "many cool ideas from great people who really care about their patients."

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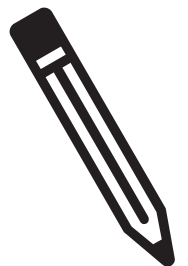
The review committee kept the process simple: a two-page application, with just a few questions about the idea, whom it would benefit, and how it

would be implemented. The application didn't even have to be typed; it could be handwritten.

So far, the Pyramid Fund seems to be the only one of its kind at an academic medical center. "A number of institutions have awards for people who come up with ideas for saving money or improving efficiency," Rand notes, "and there have always been mechanisms for getting pilot money for academic research projects. But we weren't aware of any program that really offered an opportunity for rank-and-file people, at any level, to gain funding for what essentially are just good ideas around patient-centered care: How do we improve the experience of patients and families? How do we empower anyone in the system to try and put those good ideas into practice? This was, to our knowledge, a completely novel program."

At press time, there were 45 more prospective Pyramid grants being reviewed by the committee. Hellmann hopes to fund at least two batches of proposals a year; the committee will also review how well the funded projects have worked. "Just a simple check-in," says Rand, "we want to know, how did it go, were there any problems, and do they have any suggestions for improving the process?" One measure of success she has seen already: in staff meetings throughout the hospital, good ideas are now mentioned as potential Pyramid grants.

"We are really hoping that this program will not only improve our patients' experience, but that it will help our community of people who work here feel like their ideas are worthwhile, and that their desire to improve the lives of our patients and families is valued. What we have learned from this is that the people who work here are incredibly thoughtful and want to do right by their patients, but sometimes the bureaucracy can be so cumbersome. This meets a need." ■



Asthma Travel Packs, a Comfort Cart, Wheelchair Trays, Balloons, and More...

Besides the Skyscapes, some other good ideas that won Pyramid Funds include:

- An "Asthma Travel Pack" – a backpack with equipment, medications and information to help families of kids with asthma manage the condition at home.
- Handbooks for families of people admitted to the Adult Burn Center "to provide information to decrease anxiety."
- A "Comfort Cart" of beverages for families and patients in the Emergency Department "to ease their tension" and offer reassurance.
- Gloves, room heaters, hand warmers and other aids for people in the Scleroderma Center, who "are significantly cold-sensitive," to help them have a more comfortable clinic visit.
- Extra copies of the Alcohol Anonymous "Big Book" for patients in the Chemical Dependency Unit, "to help them navigate the start of their sobriety."
- Wheelchair trays to ease the burden for patients with cardiac telemetry monitors in the Bridgeview short-stay unit (soon to be the Carol Ball Medical Unit – see Page 16) who travel to other hospital sites for a test or procedure. "This would alleviate patient discomfort or pain from carrying the monitor on their laps."
- Also in the Carol Ball Medical Unit: A helium tank and supplies, "to celebrate birthdays and holidays with patients and families and to put smiles on their faces."
- Newsletter supplies, so patients in the Community Psychiatry Intensive Onsite Services can create their own newsletter, "share their ideas, thoughts and talents with peers and learn new skills."

Quick-Changing Protein Explains Why Heart Failure Treatment Works

Listen to Jenny Van Eyk talk about proteins, and you can almost see them in your mind's eye. One protein she's been studying has the ability to change its appearance with the resourcefulness of Wile E. Coyote. This rascal "can change tack, and change color, depending on the environment," Van Eyk says. "When it's raining really hard, for example, it could put up an umbrella; it could also put it up in the sun to protect itself from heat stroke. Or it could change from an umbrella to a rain hat, to the kind of hat you would wear going to the horse races, all depending on the environment."

Let's pause here to consider that what Van Eyk is talking about is really tiny – much smaller than a cell, or even a gene. It's a protein; even more specifically, an amino acid residue (amino acids are the building blocks of protein) that makes up this protein. This one in particular is called a cysteine residue, and it's very sensitive to oxidation. It is a redox sensor; "redox" is scientist's shorthand for oxidation and reduction, and this, very basically, is a reversible chemical process involving the gain or loss of electrons. A redox sensor can read what is happening to a cell and tell if it is in harm's way.

What Van Eyk is talking about is really tiny, much smaller than a cell, or even a gene. It's a protein.



Van Eyk, Ph.D., is a pioneer in the relatively new and very complicated field of proteomics, and director of the Johns Hopkins Bayview Proteomics Center, begun by Dan Amos and supported in part by Paul and Courtney Amos. Proteomics involves taking a very complex sample of proteins in the blood, or even in a few cells, and shining a powerful laser at it. When the laser energy hits the proteins, it smashes them and throws them at a detector. When and how they land helps scientists determine their size; lighter bits get chucked further than heavier ones. Each protein makes a unique signature, or fingerprint for each of its pieces. These protein splotches also serve as snapshots that mark stages in a disease: For example, in a heart attack, certain proteins made by the heart suddenly appear in the blood. Van Eyk describes the bloodstream as a ticker tape that tells a constantly changing story of disease and how the body reacts to it.

In this case, to sum up, we have a protein that can whip out costume changes like nobody's business. Why do we need to know about this? If you've ever read the Dr. Seuss book, *Horton Hears a Who*, then you'll know that even the tiniest things matter. This redox sensor would suddenly become very important if you had congestive heart failure. For example, one effective way to treat this condition is with CRT, cardiac resynchronization therapy. CRT involves a specialized pacemaker that can multi-task: It coordinates the beating of both the heart's left and right ventricles (a pacemaker is typically implanted only in the right ventricle). When both ventricles are beating together, instead of with a delayed or off-sync rhythm, this makes the heart more efficient at pumping out blood. Patients with this device feel better, are able to exercise more, have less heart dilation, and live longer.

And yet, "nobody knows exactly why or how CRT is working," says Van Eyk. In a large collaboration study with the division of Cardiology, along with Sheng-Bing Wang, Brian Foster, Jasma Rucker, Brian

If you've ever read the Dr. Seuss book, *Horton Hears a Who*, then you'll know that even the tiniest things matter. This redox sensor would suddenly become very important if you had congestive heart failure.

O'Rourke, and David Kass, Van Eyk showed that the oxygen stress in heart failure is determined largely by the rapid-fire changing of one cysteine residue – a redox sensor – of a protein, which synthesizes an energy-producing chemical called ATP. Their work was published in *Circulation Research*. "It's under quite a novel regulation," Van Eyk says. "This one particular cysteine residue senses the environment, and the modifications switch on and off."

In heart disease, she explains, this redox sensor can become blocked – it appears to "change its clothing" – and the heart cell is hurt. But with some clinical treatments, the sensor's appearance improves, just as it seems to warn the heart that it's at risk, and protects it from damage. "What we showed was that when you have heart failure, you have one set of very bad modifications – think of a ripped and tattered shirt and pants. But when someone undergoes this CRT, the protein produces a protective mechanism – now it's a very classy tux – and it doesn't go bad anymore. In fact, it protects the protein and heart." Shedding light on how the heart regulates, protects itself, and preserves its ability to make the energy that is essential for life may eventually lead to better treatment for heart failure. ■

A true giant in academic medicine is the proverbial pearl beyond price – a treasure you do your best to keep. So when David Hellmann, M.D., Vice Dean at Bayview and Chairman of the Department of Medicine, learned that John Burton, M.D., the pioneer of geriatric medicine, was thinking of retiring, he saw a golden opportunity for Burton's "golden years:" To bring in Burton, a master clinician, as a teacher for Chief Rounds.

Every Wednesday, Burton meets with an inpatient service team that usually includes an attending physician, one or both Chief Residents, a second- or third-year resident, two interns, and a couple of medical students. He has no advance preparation; the team presents the patient at the bedside, and then they go back to a conference room and talk about that patient's particular health issues.

"It's not at all geriatric medicine," say Burton, "although geriatrics is so prevalent, inevitably it comes into play." Burton sees his role during these rounds as that of a facilitator. "I think it's good for young people to have the opportunity to present to a more senior person," he says. "It helps them to focus and articulate. There is almost always some point of controversy that comes up, and I try to facilitate that discussion. I usually add some comments where I have knowledge that would be appropriate, and then we go from there. Sometimes we're talking about the mechanism of the disease, but much more commonly about the human being who has an illness, and how they come together." It's usually more about the art of medicine than the science, he adds, "although we're doing both at the same time."

Burton likes the fact that these rounds begin at the bedside but end with a discussion away from the wards. "I think it's the right combination," he says. As a medical student at McGill University, Burton participated in rounds at the patient's bedside with a similar-sized group. Then, on the Hopkins Service of Baltimore City Hospitals, "when I was an intern, we did Chief Rounds every week, and it was the entire medical service, 40 of us with the chairman." Having a meaningful discussion was very difficult with such a big group, he recalls.

"We talk about the work-life balance for younger people, but we have not really given much thought to what we can do for older people. Many of them are giants with much to contribute, but the idea of being an attending physician, working seven days a week and weekends, has lost its luster... This solution is a win-win."

Burton returned to smaller rounds when he was a Chief Resident, and later as an attending physician, in charge of Morning Report. However, he developed a habit during those years that has stayed with him, and which he now hopes to infuse in the next generation. "I found that Morning Report tended to be 'the facts,' and not the human being," he says, "so afterward, I would go up and see the patient on the floor whom we had just talked about. And very often, I would have a totally different feel about the person, just by spending five, 10, 15 minutes visiting. It has impressed me with the critical importance of having our discussions focused on the ill human being, not just the disease."

Hellmann and Roy Ziegelstein, M.D., lead Chief Rounds the other days of the week, and Burton credits their wisdom in emphasizing this same point. "Having them advocate for this, always having the patient front and center, is very important. I wish this went on at all medical centers, but it's the exception, not the rule."

For his part, Hellmann is thrilled that Burton, who is now working half-time, has stayed to teach. "We talk about the work-life balance for younger people, but we have not really given much thought to what we can do for older people. Many of them are giants with much to contribute, but the idea of being an attending physician, working seven days a week and weekends, has lost its luster. For us, having John Burton at a place where he can have the phenomenal impact he has as a great clinician who puts the patient first through role-modeling, in a job that is compatible with his goals in life, is a win-win." ■

What is Precision Medicine, and Why Is It So Important?

What would you rather have? A big old mainframe computer, roughly the size of a Buick, with a monumental memory storage system that reminds you of that last scene in *Raiders of the Lost Ark*? Or a nice desktop computer, or a laptop? Or a smart phone or tablet? All of these tools can get you the same basic information. But which one is best for your specific needs?

Another question. You have cancer. What would you rather do, try a chemo drug that has helped a lot of people – but not everybody? Or let your biopsy and bloodwork cut to the chase by determining whether this drug will work with your particular cancer cells – and maybe save yourself some hospital time, money, and weeks of throwing up and losing your hair for nothing, when a different drug might work much better?

Medicine is increasingly coming down to choices like these, and how we respond to this challenge, Antony Rosen believes, “will determine the future of academic medicine and of Johns Hopkins.” The future, Rosen and top Hopkins leaders believe, lies in Precision Medicine – highly individualized, focused care in which subsets of patients are identified, and their treatments are tailored accordingly. Rosen, M.D., Director of the Division of Rheumatology and the Mary Betty Stevens Professor of Internal Medicine, is starting a new program in what is being called “Precision Medicine.” It will begin in Rheumatology, but he hopes that results from two pilot projects will expand to help other patients, as well.

“Precision medicine is all about patients,” says Rosen. “This is not discovery in other areas that may or may not be relevant to humans. This is discovery in patients. In order to really, profoundly change the way medicine is practiced and accessed, there needs to be a major move to precision.” Precision requires tools, systems, and infrastructure: One day, “the output of our enterprise is going to be measured by whether it’s going to change the way people are treated, the cost of treatment, cost of diagnosis and the precision of therapy. I really believe that medicine, which is already undergoing some profound changes, is going to have to be more precise if it’s going to change well.”



When Someone Has More Than One Chronic Illness

If you have diabetes, what needs to happen in your life – any dietary changes you need to make, or medications you should take, if the disease can’t be controlled by diet alone – is pretty straightforward. If you have congestive heart failure, the words “fluid overload” become very important, and your medical care becomes centered around diet, lifestyle changes, and medications to avoid this problem, which could send you back to the hospital. But what if you have diabetes *and* congestive heart failure? What if you have both of these and something else, like arthritis? You’ve got multiple chronic illnesses, and the medical rules – if there are any – that work for treating one disease may make another of your conditions worse.

You are in a club nobody wants to be in – whose membership, unfortunately, is growing. Until a few years ago, your predicament was unrecognized. Cynthia Boyd, M.D., was a fellow in geriatric medicine when she discovered this critical area of need. Clinical practice guidelines, she found, were based on the single-disease perspective. But she was seeing patients who had not only several things wrong at once, but different doctors treating each condition, “thinking about one disease at a time,” Boyd says, sometimes prescribing medicines that counteracted each other.

From a public health standpoint, there is a huge incentive to come up with better ways – as precision medicine has the potential to do – to take care of people with multiple chronic illnesses. An estimated half of all people on Medicare who have three or more conditions use 90 percent of Medicare’s annual budget. But solutions will likely be as difficult, and as individualized, as the diseases themselves, Boyd believes.

The problem in complex chronic illnesses is that “a lot of the skill that physicians develop over the course of decades is experience-based, and is highly intuitive in quality,” Rosen says. Say an experienced doctor, over many years, has seen patients with somewhat unusual manifestations, and recognizes that certain groups of patients will or won’t respond to a particular drug, will or won’t have a good outcome, and do or don’t need intervention. “This is operator-dependent, it requires lots of experience, and is difficult to generalize, because it’s an intuitive thing.”

What is best for the patient? “How do we incorporate the patients’ own wishes and priorities for their own health and lives?” says Boyd. For any intervention – any drug or therapy targeted at the symptoms of one disease – there is the potential risk of a complication that could harm something else. A medication for arthritis could worsen renal function, for example – which could be a devastating side effect for someone with congestive heart failure. The true side effects of a medication are not always discovered from clinical trials, either. “The patients I’m interested in are not usually in the trials,” Boyd notes. “When someone has multiple conditions, we are less able to predict with accuracy when the benefits outweigh the harms.”

Some drugs – for providing very tight control of glucose levels in someone with diabetes, for example – may take five years before the patient sees a benefit. “There are not great data to support doing that for someone in their eighties, and some patients may actually be harmed” says Boyd. She helps patients facing a daunting laundry list of drugs prioritize which ones will provide the most immediate benefit – medicines to help with shortness of breath, or relieve arthritis pain. “Not everything that we tell patients to do is equally important.”

Boyd hopes to start a center for multi-morbidity research, where scientists and clinicians in different disciplines can pool their efforts to treat more than one disease at a time, “so we can actually give physicians the tools they need that are relevant for these patients, including how to communicate this really complicated information in a way patients can relate to and process, so shared decision-making can occur with the patients and their families.”

In many diseases, treatment has traditionally been based on patients lumped into relatively large categories – when really, “it’s all about the nuance,” says Rosen. “So if you see a thousand patients with lupus, you’ll recognize that they don’t all have the same disease. They all overlap, but they really are not the same.” Some people with lupus, for example, also get serious kidney complications, or skin disease; others don’t. And some of those people with lupus who have the kidney complications do well with therapy, and some people with the exact same symptoms don’t. “There is this incredible variation among people who all are classified into the same group, who all technically have the same disease.”

CONTINUED ON PAGE 18

How to Brew Good Ideas

Rich O'Brien, M.D., believes that innovation and serendipity go together, and you need both to foster communication and collaboration – especially between people in different disciplines. In short, if you want people who normally wouldn't even talk to each other to join forces and work together, to tackle a problem with their combined areas of expertise, you need to get them talking. And to get them talking, you need to get them in the same physical space, at least for a few minutes at a time.



A perfect example: O'Brien is the chairman of Neurology. His laboratory is on the fifth floor of the Mason Lord Building. Antony Rosen, M.D., chairman of Rheumatology, has the lab next door. If this were a fifties sitcom, one of them would have come over asking for a cup of sugar. Instead, next best thing, they kept bumping into each other – in the elevator, in the halls – and started talking about what they were working on. A few months later, the two labs split the cost of equipment together. Eventually, their two departments, along with Pulmonary Medicine, led by Landon King, M.D., collaborated to start the Myositis Center, whose multidisciplinary approach has been, says O'Brien, "a rip-roaring success."

"The Myositis Center had its genesis in the fact that we just happened to have labs next to each other and got to know each other well," says O'Brien. "There are interactions that happen because of physical proximity, and these proximities make a huge difference in fostering collaboration."

O'Brien, who with Rosen and King sits on the Advisory Board of the Center for Innovative Medicine, wants to help make more of these collaborations happen. He believes the successful future of academic medicine depends on it. "What we need around here is a coffee shop," he says, "a place where clinicians and scientists can congregate, where accidental interactions can happen between people who normally wouldn't talk to each other."

Until the architecture catches up with O'Brien's dream, he is creating virtual coffee shops with a Conversation Series, an hour equally divided between a lecture – the most recent one was given by Ron Peterson, President of the Johns Hopkins Health System – and plenty of good food. Schmoozing is encouraged. "We've done five of these now," says O'Brien. "I think it's been helpful, but we have more work to do. These interactions need to be more daily rather than just every few months."

"Most of us are still pretty silo'd off, in our own labs. We go somewhere to eat lunch, and at the end of the day, we haven't had any ideas that extended beyond our own area, because we are not being challenged by people with different perspectives. That's the kind of thing that we need to promote here."

Collaborations, in my experience, are born out of meeting people and developing new relationships." It's not unlike – pardon the neurological metaphor – encouraging areas of the brain that don't normally talk to each other to start chatting.

"All you need to do is start talking."

"Most of us are still pretty silo'd off, in our own labs," O'Brien says. "We go somewhere to eat lunch, and at the end of the day, we haven't had any ideas that extended beyond our own area, because we are not being challenged by people with different perspectives. That's the kind of thing that we need to promote here. In academic medicine, interactions between clinicians and scientists are more and more crucial, and they tend to happen most successfully by accident."

O'Brien knows how busy his colleagues are; he's busy, too. "People are feeling so tied down by their own time constraints, their families, their research careers, it's hard to make time for new things," he says. "Everyone's thinking from day to day, and it's not easy to fit new things into their calendars. But say you're sitting somewhere eating lunch, and someone introduces you to someone you don't know, whose work is not that distant from what you're doing. All you need to do is start talking." ■

When Putting Patients First Means Thinking Years Ahead

So, you've just been named Johns Hopkins Medicine's Vice Dean for Research, and the job is huge: The School of Medicine has topped the nation in NIH biomedical funding for nearly a generation, 17 years, receiving \$438.8 million last year alone. There are entire countries with smaller budgets and a whole lot less technology. What do you do now? Going to Disneyland – the proclaimed choice for winners of the Super Bowl and World Series – is out, although maybe it crosses your mind.

The first thing that Landon King, M.D., did when he got the job was some schedule juggling, making room for this hefty new responsibility in addition to his others, which include being director of the Division of Pulmonary and Critical Care Medicine. Now, he's had a few months to settle into his new role. Where is Johns Hopkins medical research headed? As a member of the Center for Innovative Medicine's Advisory Board from its inception, King has spent many hours thinking about this, and about academic medicine in general. The CIM's motto is, "Medicine is a Public Trust," and its cornerstone is the Pyramid model, developed by David Hellmann, M.D., in which the traditional "triangle" of academic medicine – teaching, patient care, and research – is fleshed out. The patient and community are at the pinnacle, with all the staff members as its foundation, each contributing to the goal – and, in the process, feeling part of something special. The Pyramid encourages collaboration among clinicians, scientists, nurses and staff. It is a dynamic, creative model designed to transform the way all

the people involved in academic medicine think about what they do.

Recently, we asked King to share his thoughts about his new position. Here's some of what he had to say.

The primary mission of the CIM is to put the patient first. How does this work in a massive research enterprise, especially when much of what's being done is at the very basic level, and many scientists will never lay eyes on a patient?

At the level of an individual faculty member, putting the patient first is easy to envision, really sort of an intuitive concept. When you're thinking about the research mission more broadly, putting the patient first is still a critical message, but now, we're also talking about patients at a distance. People who are doing basic investigation may never come in contact with a patient, and yet the motivation for their work is to advance our understanding, or identify specific new possibilities for therapy for a particular disease that patients have. So at an academic center, putting the patient first is not limited to thinking about the patient right in front of you. If we narrowly define putting the patient first as only thinking about that immediate patient, then we will have missed the mark. We definitely will have missed the mark of academic medicine.

How can you encourage scientists to think about advances that could take years to make happen?

You don't have to encourage them – that's what they think about every day! In fact, that's actually where they live, in the future, because that is the nature of basic or clinical investigation. For example: If I'm studying resolution of acute lung injury, ARDS, in the intensive care unit, and we're trying to understand how that happens and how one can intervene, even if our group finds something interesting today, there will be years' worth of work to sufficiently define those observations in a rigorous way, and extend them to the point of becoming a therapy. If I measure something in tissue response in a mouse or a human that I think could be helpful as a biomarker of the presence and absence of a disease, or the activity of a disease, there are usually years of work required before it might result in a diagnostic test. In some categories, maybe that's only a few years, in others, it could be

10 years or more. A big push at the NIH is, how do we think about the process of doing science in such a way that we can accelerate that translation from observation and discovery to implementation and clinical medicine? How do we shorten that timeline? That's the subject of a lot of conversation.

With changes in government funding of research and patient care, there's a new emphasis on pragmatism – saving money, eliminating anything considered unnecessary. Do you foresee a shift in research away from what you just described – from working toward advances that could be helpful many years down the road, and looking at more immediate benefits?

We can't let that happen. Putting the patient first at the level of the leadership of Johns Hopkins Medicine falls down if the focus is only on what's happening with the patient right in front of me; education makes no sense, and much of the research then makes no sense. Absolutely, we have to think in a very intensive way about how best to partner with patients right now to improve their care – absolutely, it means that. But putting the patient first has to mean something in addition to the immediate need, or frankly, the whole notion of the Pyramid falls down. Because you would allocate your time and effort in a very different way. Putting today's patient first doesn't advance the science of medicine, doesn't identify new therapies, doesn't identify new diagnostic approaches, doesn't really speak to careful analysis of all the things that we think could be made better – things we may think of intuitively, but have not yet proven.

If we get too ruthlessly pragmatic, it will be extraordinarily short-sighted, and we won't improve health care. There's a lot we don't know that is important to making real advances in diagnosis, in manage-

Our charge: To create an environment in which the promise, excitement and appeal of discovery and impact continue to be attractive to smart, motivated young people.

ment of disease. We are not ever going to know it unless we invest in the discovery and innovation and implementation that will allow those advances to be realized. So, one message is, we can't roll over and play dead to a narrowly defined utility.

The NIH budget tends to wax and wane every few years. How do you see the availability of NIH funds in the near future?

The budget has had its low points, but then for a five- to six-year period in the mid 1990s, it fundamentally doubled. Since then, it's been flat – and a flat budget with any inflation is tantamount to a decrease. It is widely anticipated that research support may become more constrained, although the House budget proposal has a 3.3 percent increase in NIH funding. There's no question that times are tighter than they were. Paylines have gone down at every level – junior- and mid-level faculty, even highly successful senior investigators are having increasing difficulty getting their proposals funded. It's very difficult to imagine that there will be substantial relief from that any time soon.

Do you worry that this will affect the next generation of college students thinking about careers in medical research?

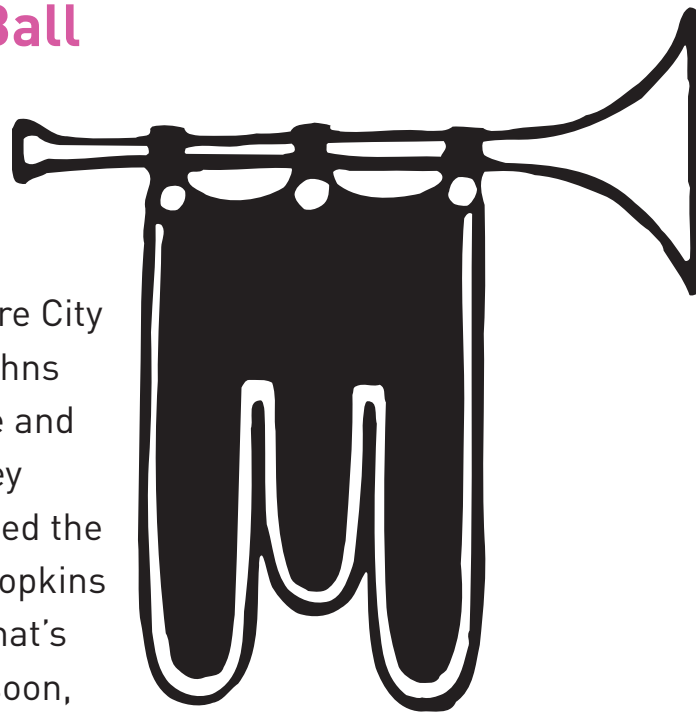
As young people make decisions about what they want to do, they are likely to think about not only whether they're stimulated and excited by a particular area, but about what the available opportunities are in that area, and about how difficult or achievable development of a career in that area might be. And right now, there's a lot of messaging that suggests research is pretty tough, the climate is really tough, and the prospects don't look better for some time to come. So, I think it's certainly possible that it's more challenging for a young person to look at a potential career in science and say, "Aha! That makes sense, that's where I want to be, that's where I want to make my mark!" The flip side of that is, very specifically, that the charge many of us have is to help create an environment in which the promise, excitement and appeal of discovery and impact continue to be attractive to smart, motivated young people. Because the rewards of devoting your life to this field can be amazing. ■

It's Official: New Unit to be Named for Nurse Carol Ball

When Carol Ball, R.N., M.A.S., came here in 1964, fresh out of nursing school, "here" was Baltimore City Hospitals. Then, in 1984, Johns Hopkins took over the place and renamed it Francis Scott Key Medical Center, then changed the name again, to the Johns Hopkins Bayview Medical Center. What's in a name? A lot: Because soon, for the first time, a hospital unit is going to be named after a nurse – and that nurse is Carol Ball.

"Putting the patient first requires great nursing," says Vice Dean and Chairman of Medicine David Hellmann, M.D. "We wanted to pay tribute to the importance of nursing in general, and to the career of Carol Ball in particular. Traditionally at Hopkins, units are named after distinguished physicians. What better way to demonstrate our commitment to nursing excellence and to collaboration than to break with tradition and name one of our important medicine units for a nurse who epitomizes commitment to compassionate and attentive care?"

Of course, says Ball, if anyone had told her back in those early days as a staff nurse that the hospital would be naming a unit for her, "I'd have thought they were crazy." But Ball's career has evolved with the hospital, as she worked her way up from being an emergency room nurse into a management role as a head nurse, then a supervisor, then a director, and now Senior Director of Nursing. The changes she has



seen, she says, have been "astonishing. What makes me so proud is, I've been a part of those changes. I've had a role in helping us move forward."

When Baltimore was in charge, "the city government was not good at running hospitals," she recalls. "To say that we were tight was not the word; we had old facilities, and old equipment." Then Hopkins took over. Ball worked with new president Ron Peterson to do a full assessment of the hospital's strengths and find out what the needs were, and helped smooth the transition. "For the staff, it was a major change, going from the government to the private sector," Ball says. "There were a lot of feelings that we had to deal with," along with big changes in benefits, and "people get upset when you do that. Our first challenge was to stop losing money." Ball worked with Peterson and the

"The goal was always to move forward, even when money was extremely tight. We really did have to work together as a whole team."

hospital's administrators to look at how the hospital could stay within its financial capability and yet still improve. "The goal was always to move forward, even when money was extremely tight. We really did have to work together as a whole team."

Ball has gotten things done over the years through collaboration, and also through patience, diplomacy, and sheer tenacity. Several years ago, her colleague, Terry Bennett, nominated Ball for an award for advancing and leading the profession, saying in part: "through her loyal leadership, the nursing department has succeeded on multiple levels. Ball builds and justifies the patient care budget and advocates for nursing department needs, so the professional caregivers at the bedside have what they need to provide the best care possible." Ball, Bennett continued, "bridges the gap between finance and clinical care. She also is the person everyone turns to for help in solving a problem or managing a difficult staff member." Because Ball has watched the facility grow and evolve over the years, "she willingly shares her vast historical knowledge, bringing a different perspective to the table. She always listens and is willing to offer caring and thoughtful advice. Ball has earned the respect of staff nurses, managers, and her director colleagues."

Today, the goals continue to change, with the move to ever-shorter hospital stays and less reimbursement. "Our challenge now is, how can we be more efficient, with more cost-containment, and yet deliver the highest-quality patient care?" Ball says. "Because the revenue is just not going to be there. So how can we do more with less?"

The fun part of the job for Ball has always been "working with the staff and helping them develop. Mentoring is critical," she adds. "I don't care whether you're a nurse or administrator, one of your main goals is the development of the staff that you're responsible for. Because they're going to replace us. You should make your staff so good, they don't need you."

Ball wants everyone to know that she is not ready for retirement. Bayview, she says, "is a great place to grow." ■

It's a new, 38-bed, short-stay unit, designed as a flagship for innovation with the Pyramid (see David Hellmann's letter on Page 2) firmly in mind. "From the very beginning, this unit was designed to be patient-centered and interdisciplinary," says Eric Howell, M.D., head of the Collaborative Inpatient Medicine Service. The unit is an ideal testing ground for launching new initiatives, such as a plan to have the patient's discharge summary, the communication from the hospital doctor to the patient's primary physician, done within 48 hours – as opposed to the legal standard for doing this, which is 30 days, an interval doctors and nurses agree is way too long.

Instead of separate rooms for doctors, nurses, social workers, physical and occupational therapists, dieticians, and case managers, there's a big "room without walls," as the Director of Nursing, John Preto, R.N., M.S., calls it. "We all work together, bounce ideas off each other in real time instead of having to track somebody down behind a closed door." Patients on the unit are primarily those with chest pain or mild heart failure, most of whom only need a short time – 72 hours or less – in the hospital.

“There is this incredible variation among people who all are classified into the same group, who all technically have the same disease.”

The standard of excellent medical care must change to account for this, Rosen says, to identify those with specific subsets of disease, with individualized manifestations of symptoms – and, underlying these, the specific molecular pathways that lead to these distinct manifestations. “The critical issue now is to precisely define these subsets, and if they turn out to share a molecular basis, then diagnosis, monitoring, therapy, and prediction all are much more likely to be applied appropriately.” The best example of this right now, he says, is in the treatment of cancer, where molecular tests can help doctors match the best drug to the patient’s precise brand of tumor. “Part of the reason for this progress is that cancer requires that a piece of tissue gets taken in order to make the diagnosis,” and with innovations in technology and imaging, “this takes out some of the physician’s gut instinct about which treatment might work best and gives you very firm and clear measurements.”

Not that gut instinct isn’t a good thing. Nobody is saying that the day will come when an excellent physician can be replaced with a computer program – when someone will look at a complex diagnosis and say, “Hey, we’ve got an app for that!” Instead, says Rosen, the goal is that “it won’t just be physicians trying treatments based on what their experience has taught them might work.” It will be critical to develop the infrastructure for this new initiative, for “precisely capturing patient data and tissue samples, and processing them appropriately.” Rosen hopes that if the right clinical research tools can be developed, then many departments will be able to adapt them for their own needs. “There is great potential for economy of scale and access,” he says.

And the other side of the equation is just as important: What do the patients have to say? How do particular treatments affect them? What are their goals? Not everyone with rheumatoid arthritis, for example, wants to be able to run a marathon. For some people, simply being able to do basic acts of independent daily living, like putting on clothes, or opening a jar, would be nice. All patients deal with side effects of medications differently, as well. What is mild discomfort and inconvenience for one

person might be unendurable for another. This must be taken into account when a doctor is ordering up treatment that has such potential to affect someone’s life.

Rosen is beginning on a small scale, with two pilot projects. One involves “capturing clinical information” – which joints are involved, all the clinical features of the disease – on selectively followed patients with rheumatoid arthritis. “There is a patient-reported outcome component, where investigators will look at what various aspects of their disease do to patients,” and how they respond to their symptoms and treatment. The project will look at molecular predictors of outcome; also, investigators will use different forms of imaging – ultrasound, x-ray, MRI – to look at joint erosions, and see whether they can identify any subgroups. Anti-inflammatory drugs called TNF antagonists, used to treat rheumatoid arthritis and other diseases, are often prescribed, “and yet not everybody responds,” says Rosen. “We would like to be able to define which people are going to respond without having to give them six months of an incredibly expensive agent, and find appropriately targeted therapies of choice.”

The other pilot project, done in collaboration with the School of Engineering, is for patients with scleroderma. “Scleroderma is a great example of a disease where patients are prospectively followed and huge amounts of data are collected,” says Rosen. Many novel measurements – of cell types, and immune response markers that vary over time – are taken; some patients develop cancer, and some don’t. All of this highly detailed information will be sifted through by biostatisticians, engineers, mathematicians, computer scientists, basic investigators, and clinicians, who will look for measurable parameters that can help doctors find subsets of patients, and come up with better ways to help them. ■

Reflections on Clinical Excellence



The Miller-Coulson Academy of Clinical Excellence is one of the signature programs of the Center for Innovative Medicine. Its mission is to recognize and encourage master clinicians at academic medical centers. The Academy’s criteria are rigorous, and include an extensive clinical portfolio, an external review committee of leaders at top academic medical centers, and an internal selection committee. Its members share their thoughts on the Academy’s blog, “Reflections on Clinical Excellence,” which promotes discussion and sharing of perspectives. Here are a couple of recent entries:

Mercurial Emotions after Stroke
I was seeing “L” back in the office for the first time since he had suffered a stroke. Now age 55, he had suffered with complications of diabetes mellitus since the age of seven. Despite the development of retinopathy, neuropathy and renal failure leading to a kidney transplant, he had remained upbeat, motivated to take care of his health. Most importantly, he always found joy in life. Today he was clearly different.

The stroke had caused a large bleed in the right side of his brain. His wife had called 911 after he had fallen from sudden left-sided weakness. Initially she thought he was hypoglycemic, but his glucose was fine. Soon after arriving in the emergency room, he... required intubation and placement on a ventilator. Miraculously, he started to steadily improve over the next 72 hours (and was able to be taken off the ventilator). L quickly regained strength and was able to walk. He improved so quickly that he decided, with my support, not to go to a rehabilitation hospital, but rather to go home and receive home physical therapy.

So here he was before me with tears in his eyes, and I did not know how to understand them. We had walked from the waiting room to my office together, and his gait was amazingly normal. We had chatted while walking and he had appeared his old self. Once he sat down, his eyes had swelled with tears. I let him regain his composure and he finally explained. He had started having vivid recollections of childhood events. Several were triggering crying spells. One event, however, was dominating his thoughts: “I am four years old and helping my mom and dad decorate the Christmas tree. I dropped a light bulb and somehow it sparked. Within a few seconds, there was a fire and the tree and all the presents underneath it were in flames. My dad put out the fire, but all the presents were destroyed. I had ruined everybody’s Christmas. I was heartbroken. My mom and dad tried to reassure me that it was not my fault and that they were not angry with me. I couldn’t stop crying for days. But now here I am, over 50 years later, and I can’t stop crying over this event that all of sudden seems like it occurred yesterday.”

It was clear that somehow the stroke had activated this painful memory and made him have uncontrolled crying. He denied feeling depressed. We talked more that day and later that afternoon I scoured the literature looking to find out if there were descriptions of this happening after a stroke. Sure enough, there were several reports of post-stroke pathological crying... However, I could not find an explanation as to why he was having such a vivid recollection of a distant memory, as most stroke patients have memory difficulties.

I called him about a week later and discussed with him what I had found. He related that he was getting better gradually and was no longer crying quite as much. He felt even better as we discussed emotionality being common after a stroke. Now we are working on getting him back to work. I am sure he will succeed.

Michael Fingerhood, M.D.

Osler on Humility
The art of detachment, the virtue of method, and the quality of thoroughness may make you students, in the true sense of the word, successful practitioners, or even great investigators, but your characters may still lack that which can alone give permanence to powers – the grace of humility.

As the divine Italian, at the very entrance to Purgatory, was led by his gentle master to the banks of the island and girt with a rush, indicating thereby that he had cast off all pride and self-conceit, and was prepared for his perilous ascent to the realms above, so should you, now at the outset of your journey, take the reed of humility in your hands, in token that you appreciate the length of the way, the difficulties to be overcome, and the fallibility of the faculties upon which you depend.

In these days of aggressive self-assertion, when the stress of competition is so keen and the desire to make the most of oneself so universal, it may seem a little old-fashioned to preach the necessity of this virtue, but I insist for its own sake, and for the sake of what it brings, that a due humility should take the place of honour on the list.

Sir William Osler, who in 1889 became the first Professor of Medicine at Johns Hopkins

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"Most of us are still pretty silo'd off, in our own labs. We go somewhere to eat lunch, and at the end of the day, we haven't had any ideas that extended beyond our own area, because we are not being challenged by people with different perspectives. That's the kind of thing that we need to promote here. In academic medicine, interactions between clinicians and scientists are more and more crucial, and they tend to happen most successfully by accident."

Rich O'Brien, Chairman of Neurology and member of the Center for Innovative Medicine's Advisory Board. He has created a Conversation Series, an hour equally divided between a lecture and plenty of good food. Schmoozing is encouraged. O'Brien hopes that collaborations will follow.

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