

breakthrough

NUMBER 3 • SUMMER 2008

Forging Stronger Ties: A Road Trip to Sparrows Point

Reversing the Domino Chain

Wegener's Best Weapons

How to Talk, How to Listen

ICU, Walking Out The Door

Dementia: Much May Be Preventable



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THE JOHNS HOPKINS CENTER
FOR INNOVATIVE MEDICINE

breakthrough



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A ROAD TRIP, NEW COLLABORATIONS, IMPORTANT TALKS

In a very short time, our Center for Innovative Medicine has made great progress on many fronts. We've been telling you about them in this publication, and you can read about them on our website (<http://www.hopkinsmedicine.org/innovative/>), but I want you to know that I'm feeling a lot like I did when my wife and I watched our oldest child stand up and take his first baby steps. You believe it's going to happen, but in that moment when it actually does, you are so proud and excited, you want to tell the world.

So what's new?

- Changes in how we treat patients in intensive care, and developing technology that may allow other hospitals to follow our model.
- New understanding about what causes dementia in many people, and exciting findings suggesting that much of this may be preventable.
- An amazing collaboration of doctors, scientists, partners in industry, and national societies coming together to save a valuable training program.
- Doctors taking a field trip, putting on hard hats, and walking around one of the world's largest steel manufacturing plants, just to get a better understanding of where their patients come from.

You can read about all of these, and more, in this issue of *Breakthrough*. But I wish you could have been at a special Grand Rounds we held recently, where we honored Mrs. Aliko Perroti for making possible the Aliko Initiative (See Page 3). This is changing the lives of patients and doctors; in fact, the name "Aliko" is even working its way into the medical language around here.

And I wish you could have heard some wonderful speakers. One of them was Dr. Kenneth Ludmerer, a medical historian, thinker, and author, who has twice been nominated for the Pulitzer Prize, most recently for his book, *Time to Heal: American Medical Education from the Turn of the Century to the Era of Managed Care*. He is brilliant, insightful, able to cut to the heart of an issue, and not afraid to say what he believes. Many of his ideas on what's wrong with academic medicine, and how to fix it, are reflected here at the Center for Innovative Medicine. Dr. Ludmerer is our very first Aliko Perroti Visiting Professor of Medicine.

Another very important talk, at the Fifth Annual Miller Lecture, was given by Dr. Holly J. Humphrey, a nationally renowned leader in internal medicine. Dr. Humphrey is also Dean for Medical Education at the University of Chicago, and in that role, she has managed to accomplish the unthinkable: She has persuaded the University of Chicago's medical school to reduce class size from 112 to 88. This is a bold move – particularly coming, as it does, when the American Association of Medical Colleges has just asked each medical school to *increase* class size by 30 percent. Instead, Humphrey believes, as we do here at Johns Hopkins Bayview, that to become excellent physicians, medical students need two things very much – extra time, and extraordinary teaching and supervision.

The Miller Lectureship is provided by the Miller Family, and Dr. Humphrey's talk was made even more meaningful by the fact that many members of this remarkable family, who care so deeply about medical excellence, were able to attend, including Mrs. Anne Miller, Mr. Thomas Miller, Ms. Sarah Coulson Miller, Ms. Leslie Miller, and Mr. Frank Coulson.

David B. Hellmann, M.D.

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BREAKTHROUGH is published by The Johns Hopkins Medical Institutions, Baltimore, MD 21287-2101.

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Design: Claude Skelton Design

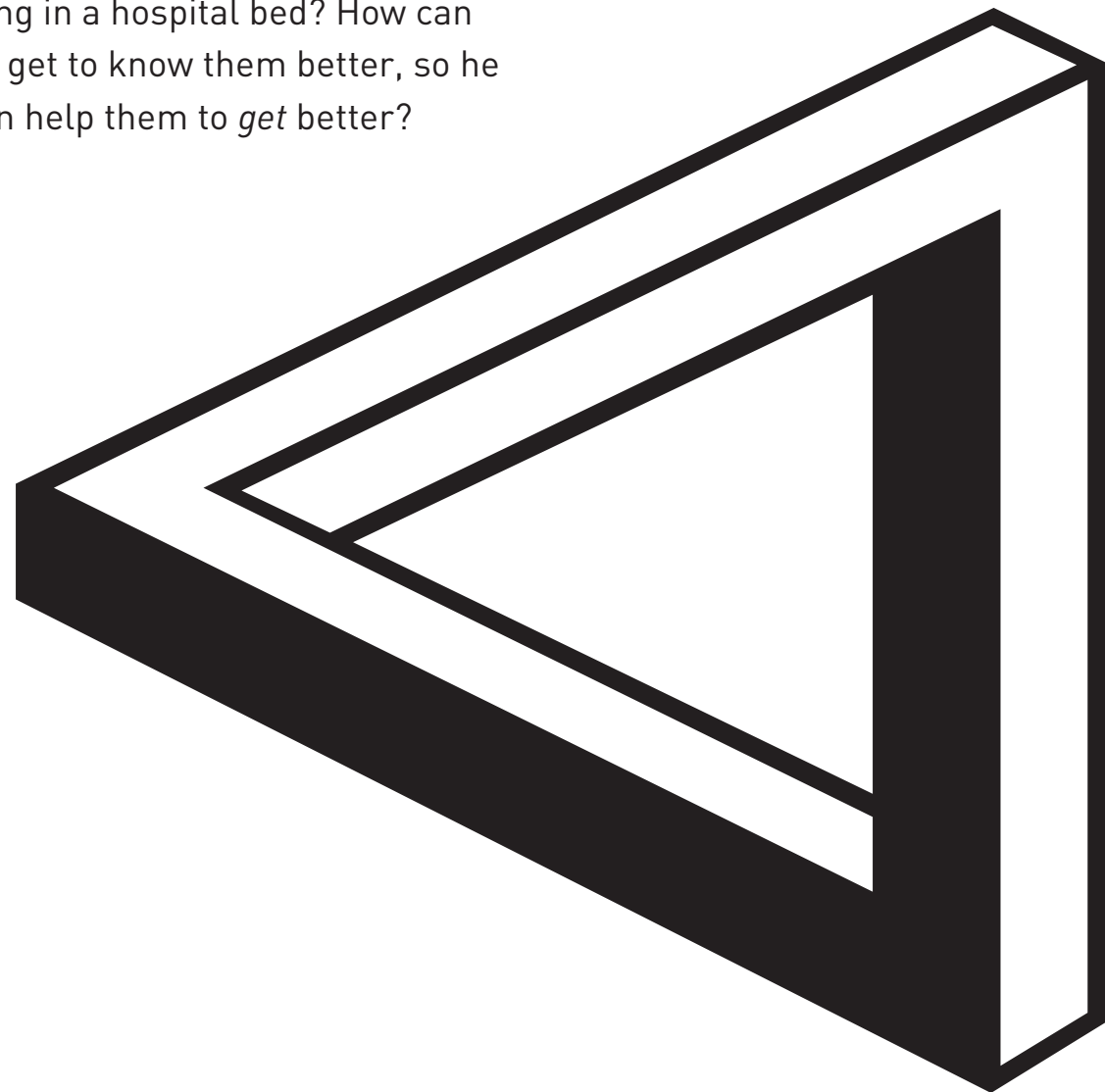
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Forging Stronger Ties: A Road Trip to Sparrows Point

Question: Why did the doctor put on a hard hat? Answer: So he could see his patients better. This sounds like a riddle, but to Adam Possner, a second-year medical resident, the real riddle is his patients. What are their lives like? What do they do when they're not lying in a hospital bed? How can he get to know them better, so he can help them to *get* better?

Questions like these are why, not too long ago, Possner and a half-dozen colleagues left work for half a day and went on a field trip to Sparrows Point, home of Bethlehem Steel – at one time, the largest independent steel mill in the world. Many of Bayview's patients are connected to the massive plant, which once employed 30,000 people, made guns and ships for both World Wars, and whose blast furnaces churned out millions of tons of steel. The plant closed in 2002, reopened with new owners, and despite rocky times still employs more than 2,000 people and produces more than 3 million tons of steel a year.



“William Osler said it is much more important to know what sort of a patient has a disease than what sort of a disease a patient has”

“We can read about these places,” says Possner – and he has (in fact, he recommends a book about Sparrows Point, called *Making Steel*, and has invited its author, Mark Reutter, to speak with the house staff). “But it doesn’t compare to going there and seeing it – so we can not just connect with our patients, but understand their perspective.”

The field trip, says David B. Hellmann, M.D., the Aliko Perroti Professor of Medicine, is a fine demonstration of what the Aliko Initiative is all about. “William Osler said that it is much more important to know what sort of a patient has a disease than what sort of a disease a patient has,” Hellmann notes. “Adam’s efforts are translating that spirit into practical ways in which we know the stories of our patients.”

As a rule, doctors don’t get out much, especially young doctors in training – although Bayview residents venture out of the hospital more than most, thanks to the pioneering House Call Program. As part of this, Possner was visiting one of his patients who lives near Sparrows Point, a company town built in the 1890s to house steel workers and their families. Afterward, finding himself so near the plant he had heard so much about but never seen, he drove up to the main office building of Bethlehem Steel, and walked in. “I’m not bashful,” he explains. “It’s amazing what you can do just by asking.” With the help of Jean Fraser in the plant’s public relations office, he organized a tour of the mill for his colleagues at Bayview. (More people wanted to go but couldn’t change their schedules, Possner notes; this trip’s audience included interns, residents, attending physicians, and a social worker.)

It was a huge hit on both sides, and Possner hopes to make this a regular event. “They did so much for us,” he says. “They really appreciated the fact that we care about our patients, and want to learn about them.”

The Aliko Initiative allows residents to spend one month not pressed for time, with fewer patients, whom they get to know well. (See *Breakthrough*, Fall 2007, available online at www.hopkinsmedicine.org/innovative) The care extends beyond the hospital; residents visit patients in their homes, accompany them on visits to the pharmacy and rehab, and may even go with them to their first appointment with their community physician. They come back with stories – discoveries they never could have made just sitting at the patient’s bedside. Sometimes the discoveries are staggering. Sometimes, they involve cats. Here are two such tales:

The case of Mr. X: Mr. X is a brittle diabetic in his thirties. He has been hospitalized repeatedly – almost 20 times within the last two years – for diabetic ketoacidosis, a potentially life-threatening complication that often requires intensive care. His doctors looked for a likely cause – something like an infection, for instance – and couldn’t find one. “The other possibility was that he wasn’t taking his insulin,” says Roy C. Ziegelstein, M.D., executive vice-chairman in the Department of Medicine and associate program director of the residency program in internal medicine. “The assumption was that this had to be the case, because he was coming in so many times.”

Although Mr. X kept coming in to Bayview, he never stayed long enough for his doctors to get to know him; his average hospitalization was a day and a half – the all-too-common, modern medical version of a Jiffy Lube tune-up. In and out. Outpatient visits were scheduled, but he didn’t show up. Mr. X was believed to be the classic “noncompliant patient.” He received a psychiatric consult, as well, to rule out depression as the cause of his noncompliance.

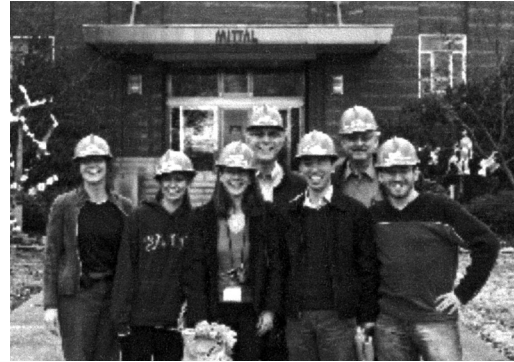
Then Mr. X was hospitalized on the Aliko service. When he went home, his Aliko resident came to visit, and received a shock: Mr. X was “most certainly not depressed,” says Ziegelstein. “In fact, he was quite happy. He was really more engaged in his health care than anyone had thought, and he wanted to control his diabetes.” But the diabetes, in his case, is so brittle that even small changes in his diet were resulting in poor blood sugar control. The Aliko resident pinpointed another possible cause of infection – when he happened to notice that Mr. X’s cat was licking his insulin bottle. That’s the cat part of this story. *Continued on Page 5*

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And why was he a no-show at his clinic visits? It turns out there were two very good reasons, neither of them being a lack of interest. He had to care for his child, and he didn't have transportation. The Aliko team worked with a social worker, who arranged transportation to help him get to his outpatient visit. "He formed such a bond with doctor who took care of him on the Aliko team," says Ziegelstein, "that he began calling her in the morning, to say, here's my blood sugar count. What should I do?"

And Ms. Y: Ms. Y had some mild retardation, some mental illness, and a terrible diet; basically, she had pared down the food groups to one: Hamburgers. "She became nutritionally deficient," notes Ziegelstein, and was hospitalized with multiple neurologic problems stemming from vitamin and nutritional malnourishment. The Aliko team took care of her, and when she left the hospital, went to see her at an outpatient rehab facility. The physical therapist reported that Ms. Y was "very difficult to engage in physical therapy. The therapists had almost given up. They thought she would probably not get stronger and be able to regain her independence."

But this is a cat story. The Aliko team remembered, because they had spent a lot of time talking with her, that Ms. Y loved her cat. They also remembered that her biggest wish was to go back home to be with her cat. "While she was lying there, they said, 'Can you show us what you would do if your cat jumped in your arms right now? How would you feed her? How would you pet her?'" And Ms. Y started using her muscles to show them. Now the cat is there, in spirit, at every PT session. And Ms. Y is getting better.



They got to keep the hats. Here's the first Bayview-Sparrows Point tour group. It was such a great experience, Possner says, that he hopes to make it a regular event. Back row, from left: Jonathan Zenilman, Sheldon Gottlieb. Front row: Susan Burgert, Amanda Tiffany, Lynda Davis, Benjamin Tu, Adam Possner.

CONTINUED FROM PAGE 4 Here's some of what they've learned: "The people who work there are giving their blood and their sweat, just as we do in the hospital," says Possner. Also, steelworkers have their own set of health problems. Conditions are much better now, but many older veterans of the plant suffer from asbestos exposure, and from exposure to extremes of heat and cold; they also are prone to heart disease, chronic obstructive pulmonary disease, and lung cancer.

Already, the trip has paid off with Possner's patients, like the man who had worked at the plant for more than 35 years. Possner started talking about the furnaces he had just seen, "and the man's eyes lit up. He and I formed a connection within five minutes that I haven't had with some of my patients that I've seen 10 times in the clinic. We forged a bond," he adds, "that really went a long way to establishing a rapport, and him trusting in me, and our coming up with a medical plan together."

ALIKI IS NOW A VERB

Google recognizes the Aliko Initiative. It pops right up, this groundbreaking program we've just started. But Mrs. Aliko Perrotti's name is also finding its way into the culture of Johns Hopkins medicine. "What's amazing to me," says Cynthia Rand, Ph.D., Co-Director of the Aliko Initiative, "is how quickly and extensively the term 'Aliko' has crept into our Bayview language as a distinct, meaningful verb or adjective, not just the name of a program." To "Aliko-ize" means to transform or revise. An "Aliko-like" activity puts the emphasis on the doctor-patient relationship.

But maybe the best is yet to come, Rand concludes. The best measure of success may be "when we can Google and find the term used without reference to our specific project," and instead used simply to mean, "actions and behaviors which result in knowing your patient as a person."

Reversing the Domino Chain: Helping Heart Attack Patients Faster

Take the terror of chest pain, plus all the heart attack fears that go with it, and add to that the surreal frustration of not being able to get treated right away. It happens, every day, all over the world – mainly because of an unfortunate domino chain that starts in the emergency room. If the emergency room is backed up, the ambulance gets diverted elsewhere.

But even if the emergency room has beds, and the patient can be rushed to urgent treatment (usually, a balloon angioplasty to open up a clogged artery), there is still potential trouble. Another roadblock – this time, no available beds in intensive care – means the poor patient has to wait again, in the recovery room, until an ICU bed opens up, sometimes for hours. It's a domino chain from hell, the stuff of nightmares, for doctors as well as patients.

Through innovative streamlining efforts, physicians have made sure this almost never happens at Bayview. Beds are available right now, because doctors are thinking several hours ahead, assigning patients to the cardiac team through the hospitalist division, led by Eric Howell, M.D., Director of the Zieve Medical Services. What's happening now is a domino chain, as well – but a good one – and this, too, starts in the Emergency Department. Last year (in the Fall 2007 issue of *Breakthrough*, available on our website), we told you how Howell and colleagues managed to speed up the flow of patients from the Emergency Department to the hospital. Through a groundbreaking triage program, hospitalists got patients admitted faster, and cut the average patient's stay in the Emergency Department by 25 percent.

Now, building on that success, Howell's service is making sure ICU beds will be available, by staying one jump ahead of the patients. "We look into the future," he says. How many open ICU beds are open? Who's in the Emergency Department? Who's coming by ambulance? "What's it going to look like in two to six hours, and what do we need to do to make sure those beds will be open then? It may seem like a no-brainer, but nobody was managing all those ICU beds proactively."

Part of doing his job well, Howell has shown, is thinking like an air traffic controller – managing the flow of patients in and out of beds, transferring patients from Intensive Care to stepdown units, "so there are always open beds, so patients can move from the Emergency Department to the Cath Lab to the ICU."

In 2006, Bayview's ICU was often full, and this is called being on "red alert." (Emergency Departments that get backed up are also on red alert, and the ripple effect is significant; ambulances don't bring patients to backlogged ERs, and beds in other parts of the hospital don't get filled.) "Two years ago, the ICU was on red alert for more than 2,500 hours," says Howell. "Every week, we were on red alert for tens of hours." The turnaround has been remarkable. For this entire year, the ICU has spent fewer than 50 hours on red alert. "It's less than 1 percent of what it was. We have virtually eliminated red alert."

Now, thanks to the available ICU beds, heart attack patients who come to Bayview can get the care they need right away. The critical interval that doctors call "door-to-balloon-time" has decreased dramatically. "That's the real crux of it," notes Howell. We were able to open up ICU beds, increase the rate at which patients got those beds, decrease the time to angioplasty for patients in the Emergency Department, and ambulances don't have to divert to other hospitals, so treatment can begin sooner. That's just good patient care."

Wegener's Best Weapons: Patients, Doctors and Scientists Team Up to Fight a Tough Disease

Stuart Levine's patients always come in with plenty of questions. Some are the inevitable ones that go along with having a difficult and rare disease. Others are the questions of partners in research, eager for a progress report: "What did my blood show?" "Have you found any promising genes?"

What's happening, says Levine, M.D., is "a terrific thing," something he finds amazing and humbling at the same time. Levine, a rheumatologist, specializes in the treatment and study of Wegener's granulomatosis, a complicated disease that causes inflammation in the blood vessels, which can restrict blood flow and damage organs. Although there are drugs, including corticosteroids and medications to suppress the immune system, treatment is not always perfect, the disease can recur, and its complications can be severe. Worse for Wegener's patients is the fact that their disease is rare, and often baffling to physicians. Few places in the world have centers devoted to this disease; fewer still have a multi-pronged research effort aimed at pinpointing its cause, and coming up with better treatments.

Levine hopes to find some of the answers by unlocking the secrets in his patients' own DNA – and his patients have been glad to help, giving extra tubes of their blood for study. "These patients are incredibly motivated, not only to get better, but to understand why they have this disease, and maybe to help others not get sick in the first place," he says. "Almost universally, they are eager and excited to participate. They really feel like they're part of something important. They understand that without them, none of this can happen."

Levine, with the help of the nearby Bayview Lowe Genomics Core, led by Kathleen Barnes, is looking at genes involved in the body's immune system, particularly in cells called peripheral blood mononuclear cells, and in neutrophils, which are like tiny Marines – plunging into areas of infection, sacrificing themselves to save others.



Using sophisticated, high-throughput gene expression technology, Levine and colleagues are comparing the expression of thousands of genes in people with Wegener's to those without the disease, and to people with other diseases. Preliminary results suggest there may be some differences in genes that regulate immune function, and also in genes that affect how immune cells talk to each other. Levine has earmarked for further study about 20 genes that appear to be particularly interesting.

The beauty of this powerful technology is that – unlike genetic researchers not too long ago – Levine doesn't have to search for a molecular needle in a haystack, desperately hoping that he'll recognize the problem when he sees it. Instead, he is able to study information from tens of thousands of interacting genetic events, and then close in on likely targets.

The center owes its existence in large part to philanthropist David Lowe, who has funded not only much of the Wegener's research at Bayview – including projects in the Vasculitis Center run by Felipe Andrade and Phil Seo – but whose generosity also helped establish the Genomics Core that bears his name. "We have a group of people all working together, each with different expertise, tackling the same overall disease process, all thinking critically, asking the right questions," says Levine, who is a Lowe Family Scholar at Bayview.

Attacking a complex disease from just one angle is a recipe for failure, says Antony Rosen, M.D., the Mary Betty Stevens Professor and the Director of the Division of Rheumatology. "If you don't come at it from many different directions, it's almost impossible to see how things fit together." Such a challenge is like a jigsaw puzzle, "where the shape of a piece can only tell you so much. You must have the context, to see that the blue piece goes here, and here's how it fits with the rest." Success on a disease like Wegener's also needs many different interactions, he adds. "What David Lowe did was to invest in people – in ideas, creativity, energy, and persistence. The clinical side and basic science aspects mesh together in a way that makes the whole greater than the sum of its parts."

The patients "really feel like they're part of something important. They understand that without them, none of this can happen."

Levine suspects that Wegener's will turn out to be the result of the body's exaggerated response to something in the environment – a virus, or bacteria, or inhaled dust, coal, silica, or other particles in the air. "I think it's likely initiated at the barriers in the body, because it affects the nose, sinuses, airways – the first line of defense against these outside invaders." Usually, the body is able to fight off such attacks, but in Wegener's, the mistakenly activated proteins and genes in these cells at the front lines don't seem able to shut themselves off.

He hopes to find a specific pathway that would lead to more specific, rational treatment – a difference in approach similar to that between a single rifle cartridge and a blast from a shotgun. "I wouldn't call any of our current therapies rational," Levine says. "They're globally immunosuppressive," and over time, this takes a toll on the body.

Although Levine has narrowed down his search for genetic answers, he's pretty sure the key won't be a single magic gene: Wegener's is too complicated a disease, affecting organs throughout the body. "If we did find just one gene, I probably wouldn't believe it," he says.

How to Talk, How to Listen: Things Cynthia Rand Has Learned

Cynthia Rand, Ph.D., a professor in the Division of Pulmonary and Critical Care Medicine, has spent much of her career working in the community, blending psychology with public health. A main focus of her research has been motivation: Why people behave in the ways they do, and how this affects the most common and costly illnesses we Americans tend to get – particularly, cardiovascular disease, diabetes, and asthma.

Behavior plays a role in all of these, she says; and treating them successfully relies on behavior, as well. Patients do much better if they can stick to a few rules. Exercise. Lose weight. Keep a close eye on blood sugar and blood pressure. Don't drink too much, and stay away from cigarettes.

It sounds so easy. Most of us know what we're supposed to do; medically, this is called "adherence." Yet, with chronic diseases, the average adherence is about half of what doctors recommend; and we're all paying for it, in many ways. "The cost of non-adherence translates to a significant number of unnecessary hospitalizations," and a staggering number of needless deaths – many millions – each year, Rand says.

"Just because something is a good idea and it would be healthy, doesn't mean somebody will do it."

Rand's simple answer? There isn't one. "Just because something is a good idea and it would be healthy, doesn't mean somebody will do it." We all have our own reasons for doing what we do. Part of Rand's job is to figure them out, try to address them, to help patients tell them to doctors, and to make sure the doctors listen and respond.

Cynthia Rand, who is also the Aliko Perroti Bayview Scholar, is so good at listening to patients, watching how they talk and listen to their physicians – and, on the other side, noticing whether their doctors are really hearing their patients, and whether their own message is getting through – that she has also been named a co-director of the Aliko Initiative. (For more on the Aliko Initiative, see Page 3.) She facilitates communication, teaching residents and medical students how to listen, and helping them know what to say.

Here are some of the lessons Rand passes on to young doctors:

Ask the Right Questions. Rand helps the house staff explore their patients' understanding of their medications: How do they take it? Is the regimen too complicated? Are the pills too expensive? Are they hard to take? Maybe somebody needs a liquid instead of a pill. Asking open-ended questions produces better answers, she adds. "Instead of saying, 'Are you taking your medications?' try something like: 'Has there been any change to the way you're using your medicine?'"

Don't Assume. Rand has spent years working with schoolchildren in Baltimore City; she has helped the schools – many of which, by the way, don't have a school nurse – learn to identify very young children with asthma, and evaluated different strategies to help students cope with the illness. She has sent educators into the children's homes to help their parents learn about asthma, helped parents learn how to talk to the pediatrician, and gone with them to visit the doctor.

In many cases, communication at the doctor visit has not been great. Some doctors assume that the patients, or their parents, know a lot more about the disease than they actually do. In return, sometimes it's like pulling teeth to get parents or patients to open up to the doctor. Spending extra time putting patients at ease,

or helping them feel empowered in little ways – like getting their questions down on paper – helps turn up important information. One parent didn't want her child to use a steroid inhaler, because she had heard bad things about steroids, and was worried about addiction. Once that fear was out in the open, it could be addressed.

See for Yourself. Where does the inhaler live? Who's got the medicine? Many people, especially kids, lead complicated lives. One boy might stay with his grandmother when his mom has to work; another child might spend a couple of nights with her father, and then go to stay with her mother. When these children need medicine, everybody needs to be on board, knowing what needs to be taken, and how often – and, not least, to know where the medicine is at all times. Seeing these patients outside the clinic or hospital opens the window to their everyday lives, in all their hectic complexity.

Listen. What did the doctor just say? Ask the patient. This is especially important for older patients, with involved lists of medicines and how to take them. "Often, when you've had a patient sitting there nodding, the words 'Yes, I understand' don't really tell you anything," Rand notes. "To ask that question is almost a waste of time, because almost everyone will say yes." Many physicians are surprised to find out how little their patients got out of a discussion. Instead, ask: "Could you tell me what you're supposed to take, and how you're supposed to take it?"

Rand also teaches in the Johns Hopkins School of Medicine. One class featured a panel of patients with a range of illnesses, ranging from an 82-year-old man with serious cardiovascular disease to a 30-year-old woman with cystic fibrosis, to a young man with sickle cell anemia. In one way, Rand says, these patients were all alike. "Every single one said, 'I want my doctor to know me.'"

"When a doctor spends a little extra time, patients appreciate it so much. People are so appreciative of time."

Walking Out the Door

The earth is flat. Smoking is good for you. Leisure suits make a man look good. There are times when conventional wisdom is just wrong. Take the medical intensive care unit. From its very beginnings – right here, 50 years ago, when Johns Hopkins Bayview was known as Baltimore City Hospital (before that, neurosurgeon Walter Dandy opened a surgical care unit at Johns Hopkins Hospital in 1928) – the ICU has been a place where patients are kept calm and quiet. This, doctors have always believed, is the best way for extremely ill people – those who can't breathe on their own, who are hooked up to various monitors – to heal.

"For a long time, the common presumption in taking care of critically ill patients has been that they do better when they are the least stressed," says Landon S. King, M.D., director of the Division of Pulmonary and Critical Care Medicine. "This has included maintaining a fairly high level of sedation, so that patients won't become agitated." Agitation, he explains, can harm someone in this vulnerable state, by raising blood pressure, heart rate, and generally overtaxing the body.

But increasing evidence, including observations by King's colleague, Jon E. Sevransky, M.D., M.H.S.,

suggests that all of this sedation has its own consequences – particularly, weakness and delirium – that may linger long after patients leave the ICU. Delirium, a waxing and waning of someone's awareness and ability to think, is turning out to be a bad prognostic marker for patients in intensive care, says King, "and the medicines we have been using to sedate patients may be large contributors to this state. So we have recognized that, in keeping patients sedated, we were potentially causing a change in their mental status that could be harmful" in the long run.

What if, some doctors are asking, we cut back on the sedation? What if we cut back on it a lot – to the point where we can begin some physical therapy, even while our patients are on the ventilator? After you get over the shock of this idea, it makes good sense. Patients who emerge from intensive care in better shape face a shorter road of recovery, and the goal of "having your life back" doesn't hover so far off on the horizon; it seems much more reachable. Promising results from Vanderbilt University and Latter Day Saints Hospital in Utah also suggest that this is where ICU care needs to be heading, King says.

To find out whether early physical therapy, including walking, could help ICU patients, two Critical Care physicians, Dale Needham, M.D., Ph.D., and Roy G. Brower, M.D., wanted to launch a new program – which, in itself, was a formidable job, requiring much collaboration. "To achieve this, we had to do a number of things," King says. "We had to change a culture, in which the prevailing view was still that patients do best when they're significantly sedated." This meant convincing nurses, respiratory therapists, house officers, and other Critical Care physicians that patients could tolerate lower levels of sedation, and that this might help in their long-term recovery. It also meant justifying the idea to, and being scrutinized by, the Institutional Review Board, and then getting colleagues in Physical Medicine and Rehabilitation to commit physical and occupational therapists to test-drive the pilot project.

Just like physical therapy and recovery from serious illness, victory in this case was won in a series of small steps. Needham and Brower wrote new guidelines for sedation, and then began to figure out and tackle the many individual pieces that

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would be necessary to bring physical therapy to patients on mechanical ventilators.

In early summer 2007, the pilot project began. Patients – even those critically ill with adult respiratory distress syndrome (ARDS) – began physical therapy that escalated as they got stronger – moving from range-of-motion activities to sitting on the edge

of the bed, to standing up, to walking. Making this happen is extremely labor-intensive, King notes.

Each time one of these patients took a simple walk down the hall, it was like royalty moving with an entourage – a nurse, a respiratory therapist, a physical therapist, someone pushing a wheelchair in case the patient needed it, plus the attached ventilator and IV pole.

The next task, King believes, is to streamline this retinue, and here's where the "wise use of technology" – part of the mission of the Center for Innovative Medicine – comes in. After a presentation by Needham, students in the Johns Hopkins Department of Biomedical Engineering have begun building "a device that will wrap all of this into a single unit, and perhaps reduce in half the number of people required to do this safely." The device will need a handhold of some sort, to support and help balance the patient; it will need to have a seat, in case the patient gets tired; shelves or hooks to hold monitors and medical devices, including gas tanks and a portable ventilator. The students have developed a prototype, and will soon start building the actual device. If it works, King hopes the technology and the philosophy behind it will spread to other hospitals.

The implications of this still-very-new project are substantial, and widespread. If patients move around sooner, and get stronger sooner, they can get off the ventilator sooner, and move out of the ICU – the most expensive place in the hospital – sooner. This will save money. If patients stay more physically fit now, they will need less physical training and rehabilitation down the road – and ideally, they can get back to their normal lives that much sooner.



Dementia: Study Shows Much of it May Be Preventable

The bad news about dementia is that once someone has it, that's it. It doesn't get better; in fact, it almost always gets worse. You can't, as they say, unring the bell; at least not yet.

But exciting new findings by Richard J. O'Brien, M.D., Ph.D., Chairman of Neurology at Johns Hopkins Bayview, and colleagues at the National Institute on Aging, suggest that it may be possible to prevent dementia in many people.

O'Brien, who is also a board member of the Center for Innovative Medicine, in a joint project with the Baltimore Longitudinal Study of Aging (see side story), has been analyzing brain tissue specimens, looking for abnormalities that might be clues to dementia.

Of the 200 brain samples in the study, some of the people had Alzheimer's disease. Alzheimer's differs from other forms of dementia for one main reason – telltale neurofibrillary tangles, seen only after death, under a microscope, by a pathologist. Basically, in highly unscientific terms, these tangles, or plaques, are tiny balls of protein trash, which clog up the brain and impede its function. Like crossed wires in a telephone network, a message intended for one place gets misrouted to another. For reasons that confound doctors, many people are found to have these changes at autopsy *yet do not develop Alzheimer's*; they live a normal life and die of something else.

Other people in the study had evidence of very tiny strokes. These are known as asymptomatic strokes – pinpoint-sized damage so tiny that, by themselves, they don't cause any noticeable problems. These strokes are silent. You can't look at someone and say, "I think she's had an asymptomatic stroke!" But under the microscope, that person's brain tissue is shown to be riddled with minuscule holes.

And some people had evidence of both – Alzheimer's pathology *and* microscopic strokes. Scientists have known that a person's risk of asymptomatic stroke goes up dramatically with age. But they didn't know, until now, that these tiny strokes can increase someone's risk of dementia. "What we found," says O'Brien, "was that asymptomatic strokes contribute a much larger number of cases of dementia than anyone suspected – up to about 30 percent of dementia in the United States," usually in combination with the brain changes characteristic of Alzheimer's disease. "These asymptomatic strokes are a very powerful determinant of who will become demented. Either problem alone – tiny strokes or Alzheimer's pathology – wouldn't cause you to become demented, but together, they do."

"We don't know how to prevent Alzheimer's disease. But we know a lot about how to prevent stroke. The idea that we could prevent dementia in nearly a third of our patients is tremendously exciting."

The implications of this study, published in the June 2008 *Annals of Neurology*, are tremendous. "We don't know how to prevent Alzheimer's disease," says David B. Hellmann, M.D., M.A.C.P., the Aliko Perroti Professor of Medicine. "But we know a lot about how to prevent stroke. The idea that we could prevent dementia in nearly a third of our patients is tremendously exciting."

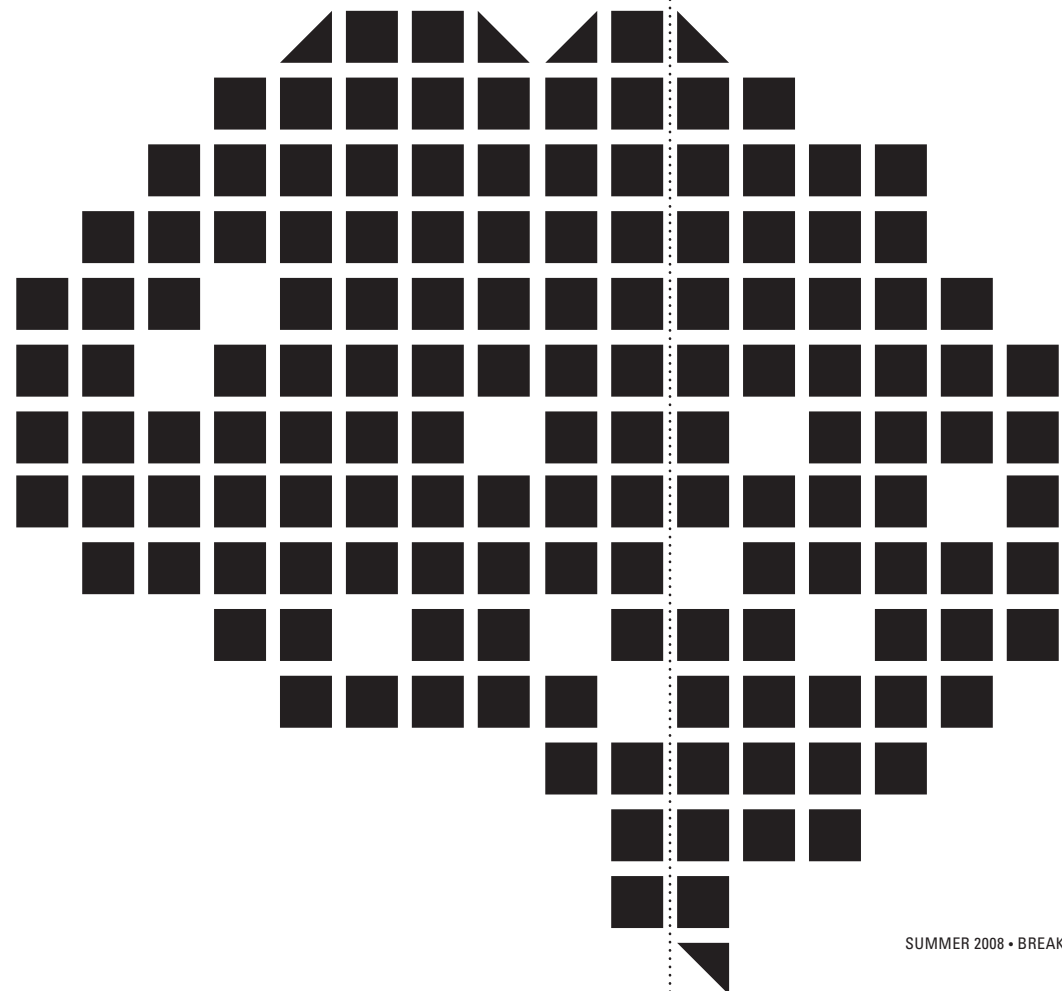
One of the major risk factors for stroke, and especially for these tiny, undetected strokes, is simply getting older. "The odds of an 80-year-old, with no other risk factors, having a stroke are higher than those of a 60-year-old with several risk factors," says O'Brien. But everyone's risk can be lowered by preventive measures: Lowering blood pressure, reducing cholesterol, improving an unhealthy diet, cutting out smoking and excessive drinking, and exercising.

Other researchers at Bayview, in a large study sponsored by the National Institutes of Health, are looking to see whether lowering the risk of stroke reduces the odds of dementia. O'Brien's research complements this, and takes it a step further. "What we're doing with the BLSA is looking at the more complicated issue of whether stroke and Alzheimer's pathology interact," he says. "Does cerebrovascular disease cause Alzheimer's pathology, or vice versa? Is someone more likely to have a stroke because of Alzheimer's disease, or more likely to have Alzheimer's because of more atherosclerosis?"

The participants in the BLSA study, O'Brien notes, were mainly white, highly educated people who had access to the very best medical care. He suspects that a broader study, of people with different risk factors and indifferent medical care, might show an even higher incidence of stroke and dementia. "That's the big question," he says. "How much dementia can we prevent, by aggressively lowering the risk of stroke?"

When you come to Johns Hopkins Bayview, one of the first things you see is a street, leading to the Gerontology Research Center, named after Nathan Shock, Ph.D. Shock was a gerontologist, the first scientific director of the National Institute on Aging, and the man who, in 1958, began the Baltimore Longitudinal Study of Aging. For half a century, the BLSA – America's longest-running scientific study of how we age – has followed the health of more than 3,100 men and women. The BLSA's massive data base, including decades of tissue and blood samples, is a unique and treasured resource for scientists of many disciplines.

Shock, widely revered, was the recipient of every major national and international award in his field. His lasting legacy, still very evident in the world-renowned Department of Gerontology at Johns Hopkins Bayview, was that he changed the way scientists think about aging – that it is not a disease, and that the things that happen as we age are not necessarily inevitable. A celebration of the BLSA's 50th anniversary is planned this fall.



Sometimes, Nice Guys Finish First

Something along the lines of an Amish barn raising happened recently in the Division of Allergy and Clinical Immunology, led by renowned allergist Bruce Bochner, M.D. For 31 years, this division has had a training grant from the National Institutes of Health, and it has given the government a good return on its investment: This group at Johns Hopkins Bayview is one of only a handful in the country consistently training residents and fellows in this field who tend to stay in academic careers.

But the recent federal belt-tightening has included NIH funding, and for the last two years, Bochner's division has had to go without its training grant. "This was a huge blow to our program, and threatened our ability to recruit and train people," he says. "We have had to scramble." But they didn't have to do it alone: Help came, willingly and gladly, from Bochner's colleagues at Bayview and elsewhere. Picture the boy ringing the farm bell in the movie, "Witness," and then see the neighbors come running. That's what happened here: The Division of Rheumatology pitched in. So did the Division of Pulmonary and Critical Care Medicine, and the Hopkins Dermatology, Allergy and Clinical Immunology Reference Laboratory. So did the Department of Medicine, "by providing support for our postdoctoral fellows, and advising us on how to revise and restructure our training grant resubmission." Partners in industry helped, too, as did two national allergy societies, the American Academy of Allergy, Asthma and Immunology, and the American College of Allergy, Asthma and Immunology. "Even our alumni, our former trainees, collectively donated enough money to fund one fellow for one year," says Bochner. "So we scrambled, and we persevered, and were fortunate to have such generous help at all levels – intellectually, financially generous colleagues to help us keep the program going."

Picture the boy ringing the farm bell in the movie, "Witness," and then see the neighbors come running. That's what happened here.

Bochner just received word that the training grant has been reinstated for another five years, but the news is even better: So much support poured in that the Division can afford to take on an extra trainee this year.

The support from his colleagues, Bochner believes, "also speaks to how wedded we all are to our mission. We are all busy people working hard to get grants, we're busy seeing patients. These training grants pay only for the salaries of the trainees; they don't pay the faculty to teach. The faculty just feels that this is so important to what we do on a day-to-day basis, that we sort of banded together to make this program get back on its feet. I'm really thankful, and proud of that."

This extraordinary effort would not have happened if the relationships hadn't already been in place. Bochner has always reached out to colleagues in other disciplines – in part, because the body's responses in allergic and immunological illnesses are so far-reaching that they affect many organ systems. His "Food Challenge" lunches (the name comes from a low-risk test to see if people have a food allergy) have a set of regulars from Pulmonary and Critical Care Medicine and Rheumatology, and invited guests from other divisions; they take turns paying for the meals – usually pizza or Chinese food. The idea came from Bochner's administrator, Janet Dorer. There is "absolutely no agenda," he adds. "Sometimes we talk politics, and sometimes we talk sports, but we always get around to science. Almost inevitably, at least one new idea or collaboration will come out of these lunch meetings. Somebody knows of somebody with a unique piece of equipment, or a unique reagent, or some patient-derived material, or special expertise in designing tests or experiments."

Such meetings, Bochner notes, are not common enough in academic medicine. "There's something about Hopkins," he says, "that attracts a lot of bright, open, collaborative people. I have visited places where everybody locks their lab drawers at night; they're very suspicious, secretive, protective of their science, their ideas, and their time." But here, he adds, "when you contact someone else, the typical response is, 'How can I help?' or 'That's a cool idea. Let's work on that together.' There is an atmosphere of scientific openness that you don't find in a lot of institutions, from the clinical side all the way to molecular research."

Bruce Bochner studies three major culprit cells in allergic disease:

Mast cells. They live in tissues, and have big granules packed with things like histamines, which get released in an allergic response;

Basophils, which are a lot like mast cells, except they circulate in the bloodstream; and

Eosinophils, which also travel in the blood but mainly dwell in tissues, where they help fight parasitic diseases. Curiously, they also show up at sites of chronic allergic inflammation – in the airways of someone with asthma, for example.

Bochner's lab has worked to understand how these cells get selectively recruited and activated – who, in the molecular world of the allergic response, invites them to the party – how they generate an allergic reaction, and how it is that these irritating cells are kept alive at these tissue sites. What business do eosinophils have in asthma? "We suspect that allergic diseases are a bit of mistaken identity on the part of the immune system," he says; "that it thinks normally harmless things like pollens, foods, dust mites and cat dander are parasitic invaders." On an even tinier level, his lab is investigating *chemoattractants*, which act like exotic perfume, luring the cells to a destination, and *adhesion molecules*, little backstage passes that allow the cells to sneak in the door.

A decade ago, as he began searching for other important molecules in these processes, Bochner established collaborations with a pharmaceutical company and a biotech company. "We discovered a molecule, on the surface of eosinophils, that's also on mast cells and basophils. As far as we can tell, this molecule is not expressed anywhere else in the body" – which makes it a good potential target for new treatments. The molecule is called *Siglec-8*, and it is a sugar-binding protein. Bochner and colleagues are trying to figure out how it works. "We've made progress on many levels, because of the ability to collaborate" with people at Hopkins, in industry, and with a super-specialized, NIH-funded "Consortium for Functional Glycomics" that focuses on sugar biology. "I sent them my *Siglec-8* molecule. They incubated it with a small chip that contains hundreds of different kinds of sugars. Amazingly, it bound to just one sugar. Now we're actively pursuing that sugar as a possible structure from which you could make a new drug."

Fixing the Lopsided Triangle: Rewarding Excellent Clinicians

The Center for Innovative Medicine began, appropriately, with a question asked by a patient. That patient was Mrs. Anne Miller, and she asked her doctor, David B. Hellmann, M.D., why there are so few excellent clinicians.

Specifically, she wondered why they didn't make 'em anymore like Dr. Phil Tumulty, a legendary Johns Hopkins clinician and teacher, who had been her doctor for many years. Hellmann took that question and ran with it. It fit right in with what he had spent his career trying to do – practice good medicine, and turn out caring physicians and astute thinkers. With Richard Paisner, he went to see Dr. Bill Brody, President of The Johns Hopkins University, and the result of their conversation was a new center, designed to create a different kind of academic medicine. Hellmann, the Aiki Perroti Professor of Medicine, is the director of that new center, the CIM.

Fast forward a few years, and welcome to a group within a center. This is the DMR project, and the letters stand for "Define, Measure, and Reward" clinical excellence. A direct descendant of that first question, this, too, has the Miller stamp – it is supported by Mrs. Miller's daughter, Sarah Miller Coulson, and her husband, Frank L. Coulson. And at the helm of this project

are four Miller-Coulson Scholars – Colleen Christmas, M.D., Steven Kravet, M.D., Samuel C. Durso, M.D., and Scott Wright, M.D. – excellent clinicians all, who know firsthand how hard it is for excellent clinicians to stay in academic medicine.

This is a universal problem in academic medicine, and it all boils down to a lopsided triangle. Most academic medical centers have some sort of triangle in their logo; it stands for the three-part mission of teaching, research, and patient care. Theoretically, all parts are equal, but it hardly ever works out that way. Only one side – research – ever gets rewarded, with grants and academic promotion.

To Hellmann, the failure to recognize and reward clinical excellence is exactly the kind of fundamental problem the CIM was meant to address. It is a curious fixture, so embedded into the culture of academic medicine that changing it must "be based on meticulous work to define clinical excellence – the kind of scholarly, rigorous effort that has been used for decades with scientific excellence."

The Miller-Coulson funding, and the creation of the Scholarships, allowed Hellmann to assemble a crackerjack team for this tough job. "It's important to get the right people on the bus," notes Hellmann. "We picked Scott Wright, because he is one of the most respected figures in medical education in the country. His 1998 article in the *New England Journal of Medicine* on defining the characteristics of a clinical role model is regarded as a classic study."

"Once in a while, you get to work on a project that you feel so strongly is the right thing. It is so important to do this, and to do it now."

Chris Durso was picked for his recognized leadership in medical education programs in geriatrics. Durso, associate professor of medicine and interim director of the Division of Geriatrics, spent many years in private practice, and brings that perspective to the DMR project. Christmas is a geriatrician and director of the housestaff program, and Kravet is a general internist and deputy director for clinical activities in the department.

"Once in a while," says Christmas, "you get to work on a project that you feel so strongly is the right thing. It is so important to do this, and to do it now."

The DMR group – officially, its name is the Clinical Excellence Initiative – has several publications in the works, most recently a paper in which they seek to define clinical excellence. Down the road, all of them hope that something lasting and career-changing for many academic clinicians will come out of this – perhaps even an Academy of Clinical Excellence, with a refereed board that would review portfolios of academic clinicians, give external validation and provide national recognition of the qualities that make for an excellent clinician.

In today's skewed system, "academic clinicians get the subtle message that they are less important," says Christmas; many of them leave for private practice. The way to get promoted is to publish, but "to get the writing done, you end up cutting back on your clinical time, so you can survive in the academic setting. The thing you're passionate about is the thing you cut back on."

Worse, says Durso, "all of this is occurring while patients with complex conditions are finding a shortage of physicians with bedside skills in diagnosis and communication." The DMR project is a venture into uncharted territory, an attempt to quantify and lay out the qualities that make an excellent clinician, and to come up with a reward system, "so that really great clinicians can be rewarded for doing great, important things," says Christmas.

The Consortium's findings have prompted further questions. Where is this sugar naturally made in the body? How does it interact with eosinophils and mast cells in tissue? The molecule seems to be present in the lung normally, but in much higher quantities in animal models of asthma. One potential new treatment targeting *Siglec-8* selectively kills eosinophils and, as an added bonus, seems to inhibit mast cells, too. Both of these characteristics would be highly desirable in any new drug for allergies and asthma.

Bochner's work has also been made possible with funding from philanthropist Hugh Cosner. "The beauty of the support from Mr. Cosner is that it allowed us to make headway in a path that has a definite clinical implication – translational research – that may turn out to be broader than we originally thought, and may lead to new treatments for gastrointestinal, skin, rheumatologic, and allergic diseases, as well."

Bochner always has his research in mind as he sees his patients, and vice versa. "Our group is very proud of the fact that while we do laboratory research, we're ultimately about helping patients with diseases, through discovery and by training new physician-scientists. It's the human condition that we're trying to improve."

"Our work, to define and measure clinical excellence, has never been done before," says Wright. The DMR group has conducted numerous phone interviews with top clinicians across the country, in addition to interviewing many gifted ones closer to home.

"One thing that strikes us," says Kravet, "is that most doctors can look back and remember excellent clinicians who inspired us. And all of us can name excellent clinicians who left the hospital, not feeling rewarded for their work."

Without the support of the Miller-Coulsons, Kravet notes, the DMR project would never have gotten off the ground. "The NIH would never fund this kind of study."

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