This is a story about tailoring treatment to patients’ individual needs. But for a minute, let’s think about shopping instead. Wouldn’t it be nice if you walked into, say, Macy’s, and your personal shopper came up to you and said, “I saw some suits that look like the cut and material you like, and I’ve put the ones in your size in the dressing room along with some accessories that would also work well with the rest of your wardrobe.” This salesperson has a finely honed idea of who you are, and isn’t just shopping for someone like you – your general weight, age, and build – but for you alone.

Now, imagine that you have a chronic disease, like rheumatoid arthritis. A bunch of other people in the world have it, and many of them take the same medications that you do. But their disease is not exactly the same as yours. How could it be? Maybe they are more physically active, maybe less. Maybe they have more pain or fatigue, maybe less. Maybe you and someone else have the exact same swollen joint, but yours isn’t bothering you. Should you be treated the same way?

A new initiative at Johns Hopkins, called “Precision Medicine,” is investigating ways to answer this question. “Precision medicine is all about putting the patient first,” says Antony Rosen, M.D., Chief of the Division of Rheumatology, who is leading this initiative. “It has the potential to make a profound change in how we monitor and treat chronic diseases.” Rosen, whose varied academic titles include being the Hugh and Renna Cosner Scholar in the Cosner Center for Translational Research and the Mary Betty Stevens Professor of Medicine, believes that moving to precision medicine is something in which Hopkins and other academic medical centers must lead the way. But to do so, he adds, means that we need to develop new tools – for measuring not only how patients are responding to treatment,
Neuroradiologist Martin Pomper is used to crossing bridges. An M.D. and Ph.D., he heads a research group that includes chemists, physicists, molecular biologists and clinicians. A professor in the Departments of Radiology, Pharmacology and Molecular Sciences, Oncology, Radiation Oncology, Psychiatry, and Environmental Health Sciences in the School of Public Health, he also directs and co-directs several centers, including one for “Cancer Nanotechnology Excellence” and the soon-to-open Center for Translational Molecular Imaging (CTMI). “Translation” is something he does every day – in working with scientists and clinicians who have their own disparate sets of jargon, and in using technology that didn’t exist a decade ago to study very small aspects of big diseases.

Molecular imaging, he believes, is an essential part of Precision Medicine. “It’s the next phase of imaging,” he says. Current imaging – X-rays, CT scans, MRI – “they’re really just photographs, snapshots in time, and that’s about 95 percent of what we do now. But what we can do with molecular imaging is actually look at the biology or physiology of what’s going on in cells and tissues in real time. We can look at things like gene expression, receptor concentrations, and mitochondrial activity.” Currently, this is mostly done in preclinical animal studies, and is not yet widely available to patients. But it should be, he adds: In cancer, “patients have tumors with different sets of characteristics. With molecular imaging techniques that are very sensitive and specific, we can pick the right patients for a particular form of therapy.” For instance, if one drug targets a certain kind of cancer cell and someone’s particular tumor does not have that target, molecular imaging tests could spare that person from undergoing grueling chemotherapy that is not going to work.

“The CTMI was developed because it’s not easy to take imaging agents from the laboratory into the clinic,” says Pomper. “We’re really geared toward taking things that have succeeded in preclinical models – discoveries at Johns Hopkins and with our collaborators from elsewhere – and moving them to the patient’s bedside.” With imaging agents, he notes, there are not only numerous government regulations that must be navigated to make sure a product is safe and effective; the product must be synthesized in a dedicated manufacturing facility according to very specific quality-control protocols.

And, after all the strict standards, what is the reward? Why is a revolution needed in imaging? Take prostate cancer: Current imaging, along with blood tests, biopsy results and other tests, can help doctors determine the stage of a man’s disease. But “now we can inject a specifically targeted molecular imaging agent into the patient, and it will light up the tumor wherever it is, and that way we can determine the extent of the disease and even begin to know a bit about its biology, or predict how it may behave in the future.” Molecular imaging can be applied to understand a wide variety of diseases. It can show the activity of drugs or the state of damage in neurological diseases such as Alzheimer’s; in rheumatological disorders; heart disease, and other ailments. It can also enable measurement of degrees of inflammation and infection at the molecular level.

“The potential is unbelievable,” says Pomper, “to use this technology for more informed clinical decision-making and ultimately, a better outcome for patients.”

but their quality of life – and an infrastructure to administer new tests and make sense of the results. “How do your patients feel that they are doing? And how do you incorporate that into your therapy? Is your therapy actually working to fix the things that are bothering the patient?”

This is why the work that rheumatologist Clifton Bingham, M.D., Director of the Johns Hopkins Arthritis Center, is just beginning has the potential to be so important. With a grant from the new, government-funded Patient-Centered Outcomes Research Institute (PCORI, pronounced “picori”) and support from Sibley Memorial Hospital, Bingham is developing an interactive way of incorporating the perspectives of patients with rheumatoid arthritis into their clinical care. “With a disease such as rheumatoid arthritis, the traditional way of evaluating how well a patient is responding to treatment has been done at a group level,” he explains, with lab tests quantifying certain inflammatory markers in the blood and other signposts, such as the number of swollen and tender joints. “But those may not really indicate how well or poorly the individual patient is doing. We have to start looking at the patient as the center of the disease. And to understand how a patient experiences the disease, we have to evaluate patient-centered outcomes.”

CONTINUED ON PAGE 10
What does this mean? Well, a doctor might see a drop in a patient’s level of an inflammation marker in the blood after a certain treatment, and think, “Aha, an improvement!” But if that medical intervention – a new drug, maybe, or a different dosage – makes no difference in how the patient feels, then “while it’s interesting what that biomarker may be telling you about the mechanism of the illness, if it doesn’t make a difference in the patient’s quality of life and ability to function, it doesn’t really help us determine whether something is effective or not.”

Traditionally, in treating people with rheumatoid arthritis, doctors have focused on pain and physical function; recently, they have looked at fatigue, as well. Bingham is developing an intricate questionnaire, to be administered on an iPad to patients in the waiting room, that will evaluate many more aspects of the disease and create “a spectrum from very bad to very good in multiple domains of quality of life,” he says. “Not just how much pain someone is having, which is what we ask now, but how does pain affect your activities? What does pain make you do differently than you would otherwise do?” The detailed questionnaire – which varies with each patient, according to how someone responds to specific questions – asks about things like fatigue, sleep, depression, anxiety, and physical function. It also lets patients describe in detail their ability to do “the things that matter to them – interacting with their family, serving as a care provider, socializing, participating in leisure activities, and work. Are they able to do the tasks at work that they need to do in order to stay employed?”

If the diseases themselves aren’t cookie-cutter, then how can the treatment be?

Wouldn’t these topics come up in a normal visit to the doctor? Unfortunately, not always, says Bingham, particularly as doctors are seeing more patients, with less time to spend in each visit. His goal is for each “domain” category – a disease-specific problem such as fatigue or pain – to be “essentially a thermometer that tells how a patient is doing in relation to the general population. What we want to study is how what the patients are telling us compares with what physicians are determining the disease activity to be. We also want to see if we can understand what is not responding to treatment, and get a better idea of why.” Alternatively, “if a physician sees that there is a swollen joint, but the patient reports that everything is going well, is that necessarily something that we need to treat?”

Bingham anticipates that this questionnaire, which can be taken online, could be valuable between doctor visits, too: “If there is a significant worsening in the degree or extent of one or more of these domains, that could signal that the patient needs to come back in. Instead of the patient saying, ‘I’m feeling worse,’ it would give us a metric, a means of tracking an improvement or a downturn.” He believes this will help patients feel that they are taking charge of their disease as they record what’s happening in daily life and how the disease is affecting it. Also, over time, “I truly believe there are going to be patterns of these different pieces of disease experience that will emerge, and we will begin to identify clusters of symptoms that relate to what is happening in the blood with the biomarkers, and in the physical exam. So it really will become true precision in how we treat our patients.”