

WHERE THE GENETICS



REVOLUTION MEETS THE PATIENT

U-M'S MEDICAL GENETICS CLINIC COUNSELS PATIENTS IN A DAUNTING NEW WORLD

The ongoing explosion of genetic information yields unimaginable potential on a daily basis and, with it, many more questions than answers, much more need than resources, and far more possibility than we've had time to consider or prepare for as a society. For those who work in Internal Medicine's Medical Genetics Clinic, the oldest such clinic in the nation, and other genetics clinics at the U-M, front-line issues – and fundamental questions – about medical conditions, ethics and rights, and navigating a rapidly expanding world of knowledge are as much a part of daily life as the patients they counsel about genetic tests and the life-altering information those tests can yield.

“Who is the patient?” wonders genetic counselor and clinical instructor of human genetics Wendy R. Uhlmann.

Until the last few years, that was a question that rarely, if ever, needed to be asked. The fact that it's on the table now is but one example of the revolution in medicine wrought by the tsunami commonly called “the genomic revolution,” as the knowledge it creates, the subspecialties it affects and the ethical issues it raises seem to increase daily.

“Is the patient the person seated in front of you, or is it other family members who may or may not be present in the room?” Uhlmann adds. “Is genetic information a personal possession or is it a family possession? And whose rights take precedence?”

She wrestles with these questions every day as coordinator of University Hospital's Medical Genetics Clinic. Uhlmann, a national leader in a still relatively new profession, is also a board member of the Genetic Alliance (an international advocacy, education and support organization for those living with genetic-based disorders), co-editor of *A Guide to Genetic Counseling*, and a past president of the National Society of Genetic Counselors.

If she doesn't have the answers, and if physicians themselves are sometimes hard put to integrate genetic knowledge into their practices, much less keep pace with its advances, imagine how daunting this all must be for patients. The complexity of genetics and genetic testing obliges all geneticists to be counselors sometimes — often to their medical colleagues — but genetic counselors like Uhlmann are the people who are specifically trained not only in the science of the discipline but also in the art of educating, supporting and serving as a resource for those hoping to benefit from it.

That encompasses a broad range of patients, says Elizabeth Petty, M.D., outpatient clinic director of the Medical Genetics Clinic, medical director of U-M's Genetic Counseling Training Program, service chief of the Medical Genetics Division, and an associate ►

professor of internal medicine and of human genetics. “Some of our patients have multiple, complex medical problems and they’ve been referred by their physicians for a diagnosis to see if we can help tie things together,” she says. “We also see patients who are thinking of having children and want to better understand their chances of having a child with a specific genetic condition. We also see patients who have a genetic disorder that runs in their family and are interested in knowing if they might develop that same kind of disease.”

Even before the patient first appears at the clinic, a great deal of work must be done. “In standard medicine,” says Uhlmann, “you can walk up to the door, take out the chart, and say, ‘Hi, Mrs. Baker,’ but in medical genetics, you need to prepare in advance to see the patient and make sure you have the knowledge that you need about the genetic condition prior to walking through that door.”

This entails several hours devoted to constructing a three-generation pedigree from family medical history, obtaining and reviewing medical records, reviewing the medical literature on the condition and the genetic testing for it, contacting laboratories that do genetic testing, completing the paperwork for the testing, and assembling information on support groups and helpful resources for the patient.

For all the headlines that genetics generates, its nuts and bolts remain a mystery to most. How do genetics work? Who needs to be tested, and why and for what? How do the tests themselves work, and what do the results mean? What should a patient do with that information, and who else should have it, and what should *they* do with it?

“Whatever knowledge you can give to patients is usually a form of healing,” says Donna Martin, M.D., Ph.D., assistant professor of pediatrics and communicable diseases and of human genetics and a clinical geneticist. “Other physicians do that too, but I think we do it even more because of the complexity of the testing that’s involved.”

A patient’s initial visit with a genetic counselor and physician takes from an hour to an hour-and-a-half. It begins with an exploration of the individual’s

Who needs to be tested, and why and for what What should a patient do with that information The questions are as legion as they are urgent.



Wendy Uhlmann

concerns, explanation of genetic factors relevant to the case, and a complete medical evaluation, followed by a discussion of all the issues mentioned above.

“When you go to a doctor and she takes blood to look at how your liver or kidneys function, she usually doesn’t explain exactly how the test is done or what she’s looking for,” says Petty. “But in predictive genetic testing, we want to make sure that people fully understand what the test results might show, what the implications of the test might be, how it might impact their life, decisions regarding having children, their employment, discrimination, insurability, and so on.”

“We’re not looking at the disease *per se*,” says Beverly Yashar, Ph.D., director of U-M’s genetic counseling training program and an assistant professor in

Human Genetics and Ophthalmology and Visual Sciences. “We’re looking at the individual who has the disease and helping them figure out how to continue to be that individual.”

Shattering myths is part of the process. For example, “There is a major misconception that risk equals certainty,” says Thomas Gelehrter, M.D., professor and chair of Human Genetics and co-author of *Principles of Medical Genetics*, a widely used textbook. “It doesn’t. Risk is risk. It’s a probability. One of genetic counseling’s concerns is how you communicate this to people so they can understand it intellectually, understand it emotionally and make a decision based on that information that’s the right decision for them.”

? How do the tests themselves work, and what do the results mean? n, and who else should have it, and what should *they* do with it?

As the number of tests proliferates, so does the need for navigational assistance. “A key point that I feel pretty strongly about is that just because a test exists does not obligate its use,” says Uhlmann. “Patients really have to think about whether it will alter their clinical care, their medical management and, just as importantly, any of their life decisions. For example, we have a test for Huntington’s disease [a progressive degeneration of the brain cells causing uncontrolled movements, loss of intellectual faculties, and emotional disturbance] and right now there is no cure, but that information can be useful for people making decisions about child-bearing, career and financial planning.”

“There are a lot of important caveats that people need to understand,” says Petty. “Having a negative test result doesn’t necessarily mean you don’t have a disease-causing mutation; it might reflect a limitation of testing. Other tests might be hard to interpret. You might screen and find a mutation in the gene associated with cystic fibrosis, for instance, but you may not know if it’s a disease-causing mutation or a normal variant, which might not have any implications for disease.”

“We know that Huntington’s disease is due to a single change in a gene,” says Uhlmann. “For a condition like cystic fibrosis, over a thousand changes have been identified in the relevant gene.”

Moreover, says Gelehrter, “A genetic test frequently gives you information that either directly or indirectly tells you something about other people in the family who have not come to you and said, ‘I want this test.’ Is there a duty to inform people about these risks? Is there a right to do it?”

Clearly, genetic counselors and medical geneticists need a high tolerance for uncertainty, not to mention intellectual agility, scientific knowledge and “people skills.” Michigan’s two-year master’s program in genetic counseling includes the study of

human, molecular and medical genetics, and counseling techniques, as well as clinical internships. It dates back to 1979, a decade after the nation’s first such program was launched at Sarah Lawrence College.

“Genetic counseling is a young profession,” says Yashar. “Its inception and development have mirrored that of clinical genetics as a specialty; we train our students with the weight over their heads that their knowledge runs the risk of

becoming outdated quickly. This isn’t new for us; it’s just the way we’ve always done it. We train our students not to say ‘how much do I know?’ but ‘what do I not know and how do I go to the primary science, to what’s happening in research, to help me gather some of those answers?’”

“What we teach here are critical thinking skills and the ability to find and understand the medical literature,” says Uhlmann. “If you’re going to enter ➤



Tom Gelehrter

the field of genetic counseling, you need to be committed to continuous learning. In some ways, that's the biggest challenge, but it's also the biggest joy. It's so rewarding to take nothing more than someone's name and some symptoms or an indication and prepare to see them; in other words, to confidently counsel about a condition that you can't spell or

There are currently about 2,500 genetic counselors in the United States.

"Is that enough?" says Yashar. "Of course not. But we can train genetic counseling students only under the direct supervision of a board-certified genetic counselor. We can't simply say we'll train six students this year, 12 next year, 18

nicians like myself are largely Caucasian. We need to encourage more students to consider genetic counseling. We're trying to reach out more into minority communities, reach out to men, really broaden the field."

"All of the genetic counseling programs in the Midwest developed a consortium



Elizabeth Petty



Donna Martin

pronounce and have never seen before. In genetics, you can't say, 'Oh, I saw a patient with this two months ago, I'm all set.' Genetic advances are occurring at such a clip that you've got to look at what happened in the intervening time."

"We're looking for independent learners," says Yashar, "people who are excited by the body of knowledge that's out there waiting to be conquered, and who also have very solid interpersonal skills, are great listeners, and really can serve the psychological sides of dealing with medical illness. It's a unique mixture."

Finding folks who are willing and able to ride the knowledge tiger is one thing. Training enough of them to meet present and future needs is quite another. The Michigan program graduates six counselors per year; the 30 programs in the United States and Canada combined turn out about 200 to 220 annually.

the following year. We can train only as many as we have appropriate educational resources for."

In other words, the number of people who can be trained is limited by the number of people who have had the training. And the situation is likely to get worse before it gets better.

Says Yashar: "As the pace at which genetic testing is being developed continues to outstrip the number of genetic counselors who are being trained, how are we going to deal with the fact that more and more genetic tests are going to be ordered by primary care physicians, who may or may not have the time or expertise to deal with the complexity of the tests?"

Diversifying the pool is one answer. "Genetic counseling is still largely a white woman's profession, like nursing used to be," says Petty. "Even genetic cli-

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to look at this a bit harder and figure out how we can change it," says Yashar. "To train as a genetic counselor is a wildly expensive proposition, and reimbursement as a health care professional in this area is relatively poor. As a result, it has been financially difficult for minorities to come into the profession because their earning potential is going to be relatively low compared to other health care areas.

"We're also working very hard to raise the visibility of the genetic counseling profession in those areas of our community that haven't even known that it existed," she adds. "It's not uncommon for many of our applicants in their 20s to say to me, 'I didn't know about genetic counseling until six months ago, and when I found out about it I realized it was a perfect fit for what I want to do in my career.'"

Other possible remedies include more education about genetic testing for ➤

“MAYBE ONE OF YOU ... ”

“I don’t feel like I’m suffering,” says Stephanie Vogt (pronounced “vote”) of Battle Creek. “There are many things that I have done since I’ve tested positive which I would never have done otherwise. I’ve started acting, which I love. I had a supporting role in one of the local civic theaters and I actually had lines. And I’m taking guitar lessons. I’ve always wanted to do that.”

Vogt’s life took on its new sense of urgency in August 2000, when she was 28. She learned at the University of Michigan Medical Genetics Clinic that she carries the mutant gene for Huntington’s disease, a progressive and fatal degeneration of the brain cells that inflicts memory and personality loss, extreme mood swings, and uncontrollable tremors and twitches.

Vogt inherited the gene from her father, who committed suicide when she was three. He had been diagnosed with manic-depression and schizophrenia, and overdosed on his medications. Years later, after Vogt resumed relations with her father’s side of the family — her parents divorced shortly before his death — she learned that she had seven relatives who suffered from Huntington’s. She began to wonder if her father had, too, and then she saw an episode of ER in

which a man with the symptoms she now recognized so well was advised to consider a genetic test for the disease.

“They knew that they were going to be dealing with information that could change someone’s life.”

“I thought I could just go into my doctor’s office and get a blood test,” she says, “but she told me there was a process.” Vogt was referred to U-M, where she and her family worked with clinical geneticist Elizabeth Petty and genetic counselor Wendy Uhlmann.

“Wendy and Dr. Petty treated me like a person from the moment I walked in,” she says. “I never felt like I was just another patient. They wanted to make sure that I actually wanted to get tested once I found out all the factors. They were both very compassionate from the

beginning. They knew that they were going to be dealing with information that could change someone’s life.”

And the lives of her family members. Stephanie’s positive test meant her father had had the gene, which increased the risk that her older sister Vicky carried it from 25 percent to 50 percent. Concerned about her insurability, and how her mother would react if both of them had Huntington’s, Vicky resisted being tested herself for almost four years.

Then she became engaged. She and her fiancé wanted to have children, so Vicky found herself back at the clinic she had first visited with her sister. Since then, Stephanie, Vicky and their mother had returned to Ann Arbor annually to tell their story to Petty’s medical students.

“Even with me being around all of this as long as I have, they didn’t want me to feel pressured,” Vicky says. “They even asked if I felt they were forcing me to do this. They are very neutral. They just want to be there for you in whatever way you need them to be there for you.”

Much to her surprise, Vicky was depressed and withdrawn for weeks after testing negative. “I figured I’d be on cloud nine,” she says. “Instead, I felt like it was almost unfair. Why Stephanie and not me?” At least, she says, she now knows that when the time comes, “I’ll be able to step up to the plate and be there for her, whether to make sure she’s in the right places to get the care she needs, or in my care if I have the ability to do that.”

It’s impossible to predict the age at which the disease will manifest itself, but “I know my family looks at me and symptom-searches,” says Stephanie. “I symptom-search myself.” Vicky worries that she’s already seen signs in her sister: increasing forgetfulness, dramatic mood swings, occasional shaking. Stephanie worries that she’ll be a burden. “That’s my biggest fear,” she says.

Their biggest hope is that a remedy will be found before it’s too late for her. The last two times they’ve spoken to students, their mother has ended their presentation by looking around the room and saying, “Maybe one of you, if you go into genetics, could be the person who finds a cure for this disease.”

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Photo: John Grap

Vicky and Stephanie Vogt

primary care physicians, what Yashar and Uhlmann call “tiered testing,” and, of course, more money.

“What I foresee happening is that we’ll start creating tiers of genetic testing based on complexity,” says Yashar. “Low-complexity genetic tests can be dealt with by primary care physicians and their affiliated health care staff. When we move into the realm of testing for conditions like cancer susceptibilities and adult onset disorders, those higher-complexity genetic tests will need to stay with genetic counselors, and it will be critical for genetic counselors to continue to educate the primary care physicians about which cases they should handle and which they should send on to us.”

The aim, says Uhlmann, “is not to turn primary care physicians into geneticists, but to help them recognize when they need to appropriately triage a case to a genetics specialist. We also need more funding to increase the number of genetics providers and training for genetic counselors and physician-geneticists,” she says. “And we need to have patients take some ownership of their health care. Part of our counseling is talking about what genes are, what chromosomes are, patterns of inheritance. As we understand the genetic basis for more genetic conditions, we’re simply not going to have time to cover all of the information for each condition a patient is at risk for in a single clinic visit.”

It’s not just the knowledge generated by genetics that is altering the practice of medicine; the non-directive and holistic approaches of its practitioners have been embraced by clinicians in all subspecialties.

“We have established a paradigm that’s becoming more common,” says Gelehrter. “We try to provide people with the information that they’re seeking and help them to make decisions that are appropriate for them. We say, ‘Here are the options, here are the possibilities, here’s what we can do.’ That’s very different from the paternalistic way medicine has been practiced for a long time. Medicine is moving toward involving people much more actively in their care, and I think that’s good.”

Because the range of problems, present and potential, that their patients present



Beverly Yashar

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runs the gamut of medicine, genetics practitioners are the natural allies of general practitioners: both are obliged to see the whole person.

“We are not in a position to ignore any organ system,” says Martin. “We have to take everything into account, just like a detective would, try to fit the pieces of the puzzle together. We rely heavily on the other subspecialties for their expertise in a particular organ system, but then we put it all together for the patients and their families.”

“One of the things a genetic approach does is make you focus on the individual rather than the disease,” says Gelehrter. “Certainly we look to commonalities, but we also have to remember that each one is expressed in a unique fashion, and the best way to treat an individual is individually.”

“Genetic counselors work in prenatal genetics, in pediatric genetics, in adult genetics, in cancer genetics,” says Yashar, “and we’re continuing to evolve as genetic knowledge makes its way into areas where it has historically not been. The newer growth areas have been neurogenetics and ophthalmic genetics, and the next big growth area will be cardiovascular genetics. That’s going to start to explode.”

“The different roles you will play as a genetic counselor really depend on the unique structures of that specialty you’re working within,” she adds. “One of the ways in which the profession is going to evolve next is that we will have more and more subspecialties within genetic counseling.”

However the profession evolves, one question frequently asked by patients isn’t likely to change soon, especially since it’s so often the hook for news stories. “It’s not uncommon for people to ask if we can change or fix the genes that aren’t working, or take out the bad genes,” says Petty. “We’re not there yet, but we’re moving, slowly, in that direction, at least for some conditions. A small percent of clinical studies of gene therapy are in phase three clinical trial, the last phase before they go into a clinical application phase.”

“The history of gene therapy is one of great hype and limited results,” says Gelehrter, who serves on the National Institutes of Health Recombinant DNA

Advisory Committee. “We review a number of clinical protocols for doing clinical gene therapy. There’s a lot of very interesting investigation going on, but there are very few success stories to talk about yet.”

Clinical geneticists and genetic counselors are firmly convinced that “all medicine will be affected by, and will use genetics in some way,” as Petty puts it. “I don’t personally think there is any disease that genetic knowledge won’t benefit in some way.”

If that’s the case, then there’s still plenty to talk about, even without a lot of gene therapy success stories: Who gets access to these tests? What tests should they have? Who decides? On what basis? How should the results be used, especially from prenatal testing? What, if anything, should everyone, or at least every member of a particular risk group, be tested for? And who will pay for this?


“Visits to the medical genetics clinic are usually covered just like any other medical visit,” Gelehrter says, “if you’re not one of the 44 million Americans without insurance. That’s our national disgrace.”

“We are at risk of widening the gap between the haves and have-nots in terms of where we’re going with genetic medicine and related reproductive technology,” Petty says. “I think we have to be very careful of risks like that.”

Care is also imperative in dealing with what she calls “the societal component of genetics. When we say there are certain genetic conditions people should be screened for, we have the potential in terms of public health practices of creating a kind of negative eugenic mind set again. We have to ask ourselves what kind of message that sends to the public about people with genetic conditions, or to the disabled community.”

These questions aren’t going to go away, any more than the genetics revolution is going to slow down.

“It’s not just up to physicians, scientists, bioethicists, or politicians to determine where genetics is going,” says Petty. “Every individual has a personal stake in genetic medicine, so it behooves us to learn as much as we can and try to figure out where and how we draw the line and how we work together as a society to use this to its best advantage to help people with disease.”

Maybe the shortage of genetic counselors and physician-geneticists relative to need is even worse than it first appears. Maybe the answer to the question “Who is the patient?” is “all of us.” 

GENETICS CLINICS AT MICHIGAN

The following genetics clinics provide services to patients within the University of Michigan Health System.

Pediatric Genetics Clinic
Pediatric Biochemical Genetics Clinic
(734) 764-0579

Perinatal Assessment Center (Prenatal Genetics)
(734) 763-4264

Neurogenetics Clinic
(734) 936-3087

Breast and Ovarian Cancer Risk Evaluation Clinic
(800) 865-1125 or (734) 764-0107

Cancer Genetics Clinic
(734) 647-8906

Medical Genetics Clinic (Adult Genetics)
(734) 763-2532

Inherited Retinal Dystrophies Clinic
(734) 763-5906