

Cracking the Cancer Code

Memorial Sloan Kettering Cancer Center

*An interview with Dr. Kenneth Offit,
Chief of the Clinical Genetics Service*

For years, science has understood that certain cancers can be inherited, winding their way through a family like an ominous thread. Now, thanks to recent breakthroughs in human genetics, doctors like Kenneth Offit, chief of Memorial Sloan Kettering Cancer Center's Clinical Genetics Service, are using this information to help high-risk individuals detect cancers early, before they appear, and in some cases to prevent them altogether.

"The notion of cancer as a hereditary disease has been known for centuries," Dr. Offit says. "And the notion that family history predisposed certain individuals to getting cancers has also been known for a very long time."

However, before the current revolution in human genetics, the search for the cause of cancer focused primarily on external factors, such as the environment, pesticides, and tobacco. It wasn't until the remarkable genetic discoveries of the past decade that scientists began to reconsider their most basic assumptions about cancer.

The Birth of Genetic Counseling and Testing

Dr. Offit remembers: "As we learned of the genetic basis of cancer through the late 1980s, suddenly cancer moved from this sort of black box — where you gave cancer-causing substances to animals and cancers appeared as a result of what we thought were environmental agents — to a fundamental understanding of what those agents did at the level of the genome."

Suddenly scientists and doctors had a language to describe classes of cancer-causing genes, and it became possible to talk about the cause of cancer. It was the beginning of an exciting, new dialogue that continues today.

"Actually, we began operating as a service before the identification of the breast cancer genes," Dr. Offit notes, referring to two genes, BRCA-1 and BRCA-2, that are thought to be responsible for most hereditary cases of breast and ovarian cancers.

In a healthy individual, BRCA-1, which was discovered in 1994, and BRCA-2, discovered a year later, are known as tumor-suppressor genes. As the name implies, their role is to put the brakes on cell division. If an individual is born with a mutation in these genes — Dr. Offit's team was responsible for discovering the most common BRCA-2 mutation — there is an increased chance that cell multiplication may proceed unchecked, leading to cancer. (Not all cancers are hereditary, but genetic defects are at work even in non-inherited cancers. A mutation causing uncontrolled cell growth can occur at any point in one's lifetime, either spontaneously, when a mistake is made during cell division, or as a result of exposure to a toxic substance.)

As a result of these discoveries and the new information they provided, the Clinical Genetics Service at Memorial Sloan Kettering Cancer Center was created, offering genetic counseling, testing, and education for individuals with high risks of hereditary cancers.

The service has gone from seeing a few dozen cases in 1993 to today's caseload of a thousand visits a year. Beginning with Dr. Offit and one genetic counselor at its inception, there are now between five and seven genetic counselors, depending on research vs. clinical allocation needs, and two full-time physicians on the service's staff, with another physician who sees patients on a part-time basis.

"The volume has increased and, of course, the major thing that has fueled the increase has been the discovery, since 1995, of all the genes signifying predisposition to the common adult cancers: breast, ovarian, colon," Dr. Offit explains.

Prostate cancer is the one remaining common adult cancer that has yet to be identified genetically, but Dr. Offit predicts the imminent discovery of its genetic source, which, like breast and ovarian cancers, will probably involve more than one gene.

Who Should Seek Genetic Counseling

The counseling and genetic testing services provided by Memorial Sloan Kettering Cancer Center's Clinical Genetics Service are typically recommended for individuals with family histories marked by multiple cases of cancer or cancer diagnosed at unusually young ages.

What to Expect

The initial one-hour to two-hour counseling session focuses on questions and concerns an interested individual has about his or her cancer risk and the risk for family members. A questionnaire filled out before the session is evaluated and a "pedigree," or a specialized chart listing a person's family history of disease, is created. Genetic counselors and physicians then provide clear and clinically relevant information, including the following: individual cancer risk assessment; personalized cancer screening recommendations and referrals; a discussion of the risks, benefits, and limitations of genetic testing; options for participating in research projects underway at Memorial Sloan Kettering; and referrals to clinicians trained to provide special counseling for individuals and families coping with the challenges that may result from genetic counseling and testing.

"It's important to note that this information about heredity and family history may or may not include genetic testing," Dr. Offit clarifies. "You can come in and get a lot of information without a genetic test. And in many cases a genetic test is something we wouldn't necessarily recommend."

Genetic Testing

"Our goal is to use genetic testing in the management of patients and their families."

To achieve that goal, genetic testing can be used preventively, diagnostically, or predictively. Preventive genetics entails testing people before they have any sign of the disease, then, if necessary, taking appropriate measures, such as changes in diet, lifestyle, and screening schedules, or preventive surgery. Diagnostic genetics can indicate the earliest stages of certain

common cancers, when doctors can most effectively intervene. And predictive genetics can provide valuable information about the course a cancer will probably take, information which in turn can help to guide potential therapies.

Dr. Offit explains: “We’ve been focusing primarily on the use of genetic testing as predictive in individuals before they have a cancer, or in individuals who have already had a cancer to help screen for other cancers they are at risk for acquiring. That’s been the mission of the clinical service.”

Implications of Genetic Knowledge

Naturally, questions and concerns about the potential benefits and dangers of this powerful new resource will be raised. Common concerns, including fear of employment or insurance discrimination, are discussed in the counseling session. Special efforts are made to ensure confidentiality of genetic information.

Increasingly, some insurance companies are even able to reimburse for this type of counseling and testing as part of a policyholder’s preventive care. In addition, genetic testing may be offered, in many cases, as part of research studies — without a cost for the test if the individual happens to fit into a certain research category.

“We try as best as we can to offer involvement in research to every individual because we still want to learn from each experience we have,” Offit says.

In the end, the service enables individuals to understand their risk, and armed with this understanding, make informed decisions.

“Ultimately,” Dr. Offit concludes, “we talk about what can be done medically and surgically to prevent or detect cancers at their earliest, most curable stages. And the part that is most exciting is that we can actually intervene in these families and hopefully we can change the natural history — which is our way of saying save lives.”