By Al Weiland, MD

The Coming Tidal Wave: Genetic Testing

A number of new technologies now exist that are likely to have a major impact on the practice of medicine over the next several years. Telemedicine is in its infancy, with teleradiology probably the most advanced.

The area that should have the greatest impact on society is the advances in genetics and genetic testing. The Human Genome Project has been underway for about 6 years, and will finish identification of the structure of human DNA over the next several years. Around 4000 single-gene disorders exist, and this project will characterize the specific location of these defects. That knowledge will provide greatly enhanced ability to provide prenatal or population screening and specific genetic therapies.

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In addition to the single-gene disorders, a lot of work is going on to characterize the interaction of many chronic and degenerative disorders that have a genetic predisposition as well as the environmental and behavioral factors that may enhance their expression. Many cancers, heart disease, diabetes, arthritides, and a number of mental and neurodegenerative disorders are in this category. Over the next 20 years or so, it will be possible to prenatally test for the *potential* to develop a wide range of illnesses during a lifetime.

Let's think about the implications of this on society if there is large-scale prenatal screening and case and carrier finding. Who will have a stake in knowing the genetic status of individuals besides the family and caregivers? How about governments attempting to prioritize budgets? Employers who want healthy, productive employees? Insurers who will write life and health insurance? Social agencies and the educational systems to plan their roles? What will happen to the confidentiality of this information? Despite laws to protect the confidentiality of HIV test information, it is now a required test to obtain most life insurance, and numerous examples of job, employment, and housing discrimination operate against people with HIV.

The implications of the work of the Human Genome Project are just being appreciated. A Working Group on Ethical, Legal, and Social Implications, has formed a Task Force on Genetic Information and Insurance. This Task Force has recommended vigorous protection of genetic privacy, while still acknowledging that insurance companies and others will probably gain access to this information.

Recently the President has proposed federal legislation to limit use of genetic testing information. Last year, nine states enacted genetic testing legislation (Alabama, Arizona, Arkansas, Connecticut, Florida, Illinois, Indiana, Tennessee, and Texas). Most of these laws ban the release of genetic test results without informed consent of the individual tested; and six ban insurers from refusing to issue or renew policies to individuals or creating differential premiums on the basis of genetic information. Some exceptions to absolute confidentiality have been recognized, such as use of the testing information for research, as long as it is anonymous and cannot be traced.

As both a very large insurer and a provider, Kaiser Permanente will have to wrestle with all the ethical, legal, moral, and social issues of widespread genetic testing. I can't think of any medical technology that could affect the lives of our children and grandchildren more.

When the Genome Project is finished, some 50,000 to 100,000 genes, and later their specific products, will be identified and catalogued. Tests will be available to pinpoint defects in single genes, and the presence, absence, or partial expression of the gene product. Rapidly, new generations of therapies will become available designed to replace defective gene products, modify their function, or stop production of unwanted proteins.

Consider the impact on the practice of medicine of having this body of knowledge available. We have a glimpse of this future with the identification of the BRCA1 and BRCA2 genes for breast/ovarian cancer susceptibility. Jake Reiss, MD, from NWP,PC led a national effort to develop a guideline for determining who should be tested in the population, and for interpreting of the results. This guideline began as a huge probability spreadsheet, covering six or seven pages of analysis and interaction of risk factors, developed in order to guide the discussion with the patient of why or why not be tested, and what a positive or negative result means. Due to its complexity the guideline was later modified to a set of recommendations to primary care providers about who should be referred for counseling and possible testing. Jake believes that lengthy discussions by trained genetic personnel will be required to review the benefits and harms of such testing. At least 4000 single-gene disorders and many chronic medical problems have a genetic component. According to John Thompson, MD, the NWP,PC chief of pathology, there are currently 140 "misspellings" of the gene for cystic fibrosis, each with a slightly different expression.

The major implication I glean from this is that the reliance on computer databases to support medical decision making will become mandatory. Large systems that can aggregate population information and make the investments to make this information readily

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available to clinicians will attract the best and brightest clinicians to the practice of medicine, not to mention create enormous value for members.

There are clearly major cost implications. I suspect only a few laboratories will have the resources to run all the very specific genetic tests, and they will be expensive. The therapies, if the few current gene-specific agents are an indication, will also be *very* expensive. Which agents are experimental, which are not; and who will be a candidate for therapy at what level of probable risk will keep new technologies committees busy for decades.

My fear is that the potential explosion in the cost of medical care, given our society's value of "I want everything possible available," will make health insurance less and less affordable, even further widening the gap between those who have access to everything, and the rest.

The third area of impact on us will be the availability of personnel trained to deal with all the genetic information and to counsel patients on its interpretation. Right now, NWP,PC is one of only four Permanente Groups with an in-house genetic service. In fact, we support our geneticist, Jake Reiss, MD, in consulting with the State of Idaho because they don't have similar resources in that state. I suspect all the Permanente Groups will have to pool resources and link them electronically to provide a consistent level of service around the country and to make sure that we are getting the best information possible to our members. There simply aren't enough training programs in the *world* to meet the potential needs.

The last area of impact I want to mention is confidentiality. Despite the current legislation in a number of states, I think there will be enormous pressure to have genetic profile information available. The line between general medical information and genetic information will become hopelessly blurred. Does your child have recurrent ear infections? Is it a result of a gene defect controlling immunologic response and therefore a pre-existing condition that will contribute to other disorders later in life? This may be a little farfetched but not very. I have no answer to the issue of confidentiality; I suspect it will be played out in the courts and the legislatures.

These issues are all a little way off in the future. They may not seem important now as you struggle through the day, or with EpicCare, our clinical information system—but they will be, and probably sooner rather than later. ❖

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Inside Microsoft's Brain

"Research is a little like conducting a dinner party. You don't interrupt the conversations and tell people what they should be saying and thinking. If you pick the right people to convene, more and better things happen than you could have planned."

Nathan Myhrvold, Chief Technology Officer
("Chief Propeller Head")
Fortune*, December 8, 1997*