

PL5 -- "THE GENE IS OUT OF THE BOTTLE: GET READY FOR THE DEBATE OF A LIFETIME!", SALON, 11/27/96

"Utter nonsense! I consider that statement to be incorrect, misleading and a great disservice to women. It's grossly irresponsible!" charged Mark Skolnick, V.P. of Myriad Genetic Technologies, objecting to a statement by a Stanford group suggesting there were no successful therapies available for the breast cancer gene for which his company markets a test. **"No known preventive mechanisms are absolutely certain. Some people don't think of the removal of body parts as an effective therapy,"** shot back Barbara Koenig, co-director of the Stanford Program for Genomics, Ethics, and Society. **"Outrageous! I think it's outrageous that he (Mr. Skolnick) is living off women!"** said Barbara Brenner of Breast Cancer Action, a San Francisco based grass-roots group.

The exchanges, generated by a reporter's attempt to find out how much hope Myriad's new breast cancer gene test offered for the 45,000 women who die it from every year, occurred on November 23 at the "III World Congress on Bioethics" in San Francisco. It was but one example of how the gene revolution is likely to touch - and upset - almost all of us in coming years.

Mr. Skolnick is probably right that scientists will discover genes for many major diseases over the next decade, including asthma, allergies, Alzheimer's, many forms of cancer including that of the prostate, cystic fibrosis, diabetes, heart disease, Huntington's disease, Lou Gehrig Syndrome, and many others. Most of us, in other words, may soon be able to discover whether we have genes likely to cause a serious illness.

To know years in advance when we would die, and how, was once the stuff of science fiction. It may soon become a reality and raise a basic question: will we want to know? If so, can the information be kept private, will we tell other family members, or face increased anxiety? If we take the test, will we risk losing our insurance or job? Will we want to have an operation or other radical

measure based upon this gene knowledge? These are only some of the agonizing questions we are likely to face in coming years.

The breast-cancer gene has become the test-case for such concerns because it is among the first disease-causing genes for which tests have been developed, and because it affects so many women: 2 million women live with it, 185,000 are diagnosed with it annually, and the number who die from it annually equals our total combat losses in Vietnam.

Mr. Skolnick's company began marketing a test to detect the BRCA-1 and BRCA-2 genes for breast cancer, at a cost of \$2400, just three weeks ago on October 30. His outburst occurred when he was asked to respond to a statement in the draft Stanford panel report that "there are no known methods for preventing breast or ovarian cancer that would be particularly important to women with mutated version of these genes."

The statement implied that even if Mr. Skolnick's test could tell a woman that she had a gene indicating a high risk of cancer, she could do little with the information. And were this true, some might argue against using this test, key to the highly-leveraged startup Myriad's success as a company.

Mr. Skolnick said there WAS a therapy available for women who learned told they had an ovarian cancer gene: removal of the ovaries. "That statement is utter nonsense," he declared. "Prophylactic oophorectomy (removal of one or two ovaries) is recommended by the National Institutes of Health for women who are at high risk for ovarian cancer. It cuts the risk of ovarian cancer from 40-60% down to a few percent. Since 70- 80% of woman die who have ovarian cancer, that could save the lives of maybe a third of those women." He clearly felt that his test could save lives by indicating to women with the gene that they should have a prophylactic oophorectomy.

Dr. Stefanie Jeffrey, described by Barbara Koenig as "a leading breast surgeon in the Bay Area," and a member of the Stanford panel, disagreed that preventive oophorectomy would be so clear a choice to

women testing positive for the gene. First, she said, not all women who are BRCA-1 positive will develop ovarian cancer; and second, some will shy away because of the potential side-effects of the operation, which produces premature menopause - making women unable to bear children, increasing possible future heart disease and osteoporosis, and causing sexual dysfunction.

By focusing on ovarian cancer, Mr. Skolnick also inadvertently confirmed the main point of the Stanford report: that the gene test added little to a woman's ability to fight the far more common breast cancer.

The exchange points up geneticists' main concerns at this point: that the publicity generated by the new genetics, and companies' promotion of testing and therapies in pursuit of profits, could lead to withdrawal of public support for gene research. "The last thing we need at this point is another Thalomid scandal," said Dr. Francis Collins, head of the National Center for Human Genome Research, a \$3 billion, 15-year project to map the human genome. Dr. Collins is highly critical of companies marketing tests to vulnerable patients at this time, and recommends that testing be limited to research settings, in which patients have given truly informed consent, and absolute privacy is guaranteed.

To some extent, some companies are listening. Jan Leschly, CEO of SmithKlein Beecham, underwrote the Stanford conference and supported its caution. He said that until now drug companies had developed drugs by looking at "function", i.e. the illness, and then going back to discover the molecular structures. Now, he said, "we are drowning in structures," i.e. genes, "and trying to find their function." He said this was a total paradigm shift, that "you will see new drugs coming to market at a rate you've never seen before." In this context, he said, his company found itself supporting government regulation for the first time in 30 years.

New startup gene companies like Myriad, however, are less publicly cautious. The fear is that their enthusiasm to market may wind up pushing people to spend thousands of dollars on tests they

don't need, encourage employers and insurance companies to discriminate against those with "bad genes", and even encourage unnecessary medical procedures. But Mr. Skolnick's response - that his test can save lives, and that slowing down its marketing can thus hurt women - cannot be dismissed out of hand.

In the heat of these passions, one thing seems clear: the gene debate is so new, the evidence for either side so slight, and even most physicians still so uninformed, that the rest of us are likely to become increasingly confused in coming years.

Neither Dr. Collins nor any of the other panelists on a "Where Do We Go From Here?" panel, for example, would answer "yes" or "no" as to whether they would themselves take the test or have an oophorectomy were they a woman with a family history of ovarian cancer. And this raised a basic question: if even geneticists and physicians are unwilling to take a clear stand on the issue, what are the rest of us to do?

This reporter left the "III World Congress on Bioethics" with far more questions than he had come with - and few answers.