RS

Nature vs. Nurture in Cancer

BOSTON — When a patient receives the diagnosis of cancer, a first question that springs to mind is: Why me?

For those with a family history of the disease, like a woman whose mother had breast cancer or a man whose father had prostate cancer, the physician offers as a facile answer, "heredity." The pernicious seeds of the tumor were presumed to be present in the blueprint of the person's DNA, drawn

MEANWHILE

at conception and programmed to blossom decades later.

For those with cancer in the lung or throat who smoked, the disease is readily ascribed to the carcinogens in cigarettes.

Although a family history of a certain cancer or exposure to a known environmental toxin like tobacco are certainly germane, they still do not fully explain why that particular individual fell ill.

Moreover, for most people with the disease, there is no apparent link to family history or lifestyle carcinogens. While we suspect that the answer is related to something in their genes or their environment, we cannot offer them a cogent reply.

Human biology has been daunting in its complexity, and out of necessity, medical science is forced to simplify it in creating concepts of illness. Sharp divisions are often drawn where they do not actually exist. Disorders are routinely categorized as being hereditary, dictated by genes, or environmental, due to ambient toxins or microbes.

By Jerome Groopman

The relative importance of nature versus nurture in illness forms the fabric of heated debate among scientists. The announcement of the decoding of the human genome last month fueled the determinist camp that contends that nature, meaning our inherited DNA, explains most pathology. Starting from this premise, scientists and biotech executives presented intoxicating scenarios depicting a direct path from deciphering our genome to the demise of virtually all diseases, particularly cancer.

We were told that we are on the brink of a clinical utopia of almost mythic character where pathology and decay are poised to be banished from our midst. As the public spirits soared, so did the share prices of genome companies.

Such heady pronouncements caused the proponents of environmental factors to bristle. It comes as no surprise, then, that a study published last week in The New England Journal of Medicine, indicating a relatively small impact of heredity compared with environment on the sporadic development of most common cancers, has been used as fodder to deflate the genomists' claims and to argue that our attention and resources should be devoted to investigating ambient toxins.

The researchers in Scandanavia compared the incidence of cancer in nearly 45,000 pairs of identical twins, who have identical genes, with fraternal twins, who share an average of 50 percent of their DNA. They concluded that environmental factors play major roles and genes relatively minor roles. The exceptions appeared to be prostate and colorectal cancer, where the effects of heredity were more prominent.

What was missing from the study was an analysis of the interaction that occurs between our genes and the world around us.

Remote from sophisticated statistics, common sense strongly argues that this dynamic interaction should be our focus. We all know of people who have smoked three packs a day of unfiltered cigarettes and lived well into their 90s without developing lung or throat cancer, or those who made alcohol a primary part of their diets and yet preserved healthy livers free of cirrhosis. We see this variability in outcome as well among women who have a powerful inherited susceptibility to breast cancer, carrying mutations in their BRCA genes. Their chance of developing breast cancer ranges from about 50 percent to 80 percent, not 100 percent.

Certainly our growing knowledge of the genome will help us make sense of this individual variability. In the case of cigarettes, we will learn which genes are important in metabolizing tobacco carcinogens in our bodies. This will be one piece of the puzzle.

Another piece will be knowledge of which genes are damaged in the airway cells by tobacco smoke, causing healthy ordered growth to cease and unleashing the wild proliferation of cancer. The amount and types of tobacco carcinogens that the individual encounters will be factored into the equation of his genes. We may then begin to explain differences in who gets sick and who doesn't.

The information gained from deciphering our genome will radically alter our long-held and largely static paradigm of the genesis of disease, particularly cancer.

Over the decades, it will become increasingly clear that the debate about heredity versus environment was miscast. Physicians will begin to craft more intelligent and complete answers to the patient's poignant question "Why me?" and offer specific advice on not only how to treat the disease but also how the environment may be altered for both the patient and the patient's family.

The author, a professor of medicine at Harvard, contributed this comment to The New York Times.