

EVALUATING CANCER IN TWINS

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Family analyses are always interesting in the study of cancer. Most cancers are not commonly felt to be familial. There are certain exceptions of course like familial colon cancer. This is not however related to the more common colon cancers seen. Patients commonly ask about the role of the environment versus genetics in the development of malignancy. But do certain families share risks of bad genes and adverse habits? Studies of twins are an interesting starting point. What are the answers?

There have been family studies of breast, prostate, ovarian and uterine cancers. It has been difficult to distinguish genetic affects versus non-genetic such as environmental or infectious.

Identical twins or monozygotic share all genes while dizygotic share 50% of genes are an informative group to analyze. A study of twins allows physicians to better examine hereditary factors but the relative rarity of twins makes cancer analysis difficult. For non-twins, this is a chance to learn. Certainly, we don't share all our siblings' diseases. Often however, I see very strong family histories - especially with prostate and breast cancer. What are the answers?

A recent study by Lichtenstein et al, evaluated twins from the Swedish, Danish and Finnish twin registries to determine genetic and environmental factors on more common cancers.

The three national registries are different in their scope. The Swedish twin registry consists of two groups including 10,503 pairs of twins of the same sex alive in 1961 who were born from 1886 - 1925. A second group of 12,883 twins of the same sex born from 1926 through 1958 exist. In the second group both twins were living in Sweden in 1972 and responded to a questionnaire that same year. Cancer was diagnosed in 4,490 people from the first group and 1,157 from the second group.

The Danish twin registry holds data on 8,461 pairs of twins of the same sex born between 1870 and 1930. It was a registry started in 1954 and later expanded to twins of the same sex born from 1911 through 1930. Annual health status was determined through 1979 by death certificates.

The Finnish twin registry included 12,941 pairs of twins born from 1880 to 1958 who were living in Finland on December 31, 1975. Malignancies were detected through a national cancer registry.

Thus overall there were 44,788 pairs of twins with 10,801 people in whom one cancer had been diagnosed.

The authors found that the twin of a person who had cancer had an increased likelihood of having the same cancer in certain instances. This was noted to be especially true for cancers of the stomach, colon, rectum, lung, breast and prostate.

For example, there was an 8% probability that an identical twin of a man with stomach cancer will have the same cancer with a so-called concordance. There were no concordant pairs observed for cancers at nine sites including non-Hodgkin's lymphoma, Hodgkin's lymphoma, cancer of the lip, oral cavity, pharynx, kidney, thyroid, bone and soft tissue.

The authors reported, "for cancers at most of the remaining sites, the concordance between monozygotic twins whether male or female, was greater than the concordance between dizygotic twins."

The authors evaluated the probability of different influences causing cancer. For stomach cancer they felt that for example 28% of the variation in susceptibility was due to inheritance, shared

environmental affects were 10% and non-shared environmental affects 62%.

The affects of a variety of diseases on inheritance or genetic factors was 35% in colorectal cancers, 36% in pancreas, 26% in lung, 27% breast, 0% uterine, 0% cervix, 22% ovary, 42% prostate, 31% bladder, 21% leukemia."

The authors noted, "the absolute risk of the same cancer before the age of 75 years for monozygotic twin of a person with colorectal, breast or prostate cancer was between 11% and 18%. For dizygotic twins who have the same degree of genetic similarity as full siblings, the risk of these cancers were 3% to 9%. These figures could be valuable in providing clinical guidance not only to twins of persons with cancer but also to other first degree relatives."

In summing up the analysis it was noted, "the overwhelming contributor to the causation of cancer in the population of twins that we studied was the environment. For some forms of cancer, in which a shared environment is important, it may be possible to find clues in studies of childhood environment or long lasting family habits. The relatively large inheritability proportions for cancer at some sites, provide the wide confidence intervals, suggest major gaps in our understanding of heritable cancer. Even for cancers for which there is statistically significant evidence of heritable component most pairs of twins were discordant for the cancer - indicating that, on the population level the increase in risk of cancer even among close relatives of affected persons is generally moderate."

What role does genetics play? And what role does environmental issues play in influencing the development of cancer? Do certain social or familial factors play a deciding factor?

Is it that we are all destined to be controlled by factors over which we have little control - like genetics? The answers seems to be that genetics is important, but unusually is it a great factor in the majority of cancers. For those who suffer a familial trait that is adverse, this news is of little comfort. An exception may be that the likelihood of passing it on to future generations - our children - may well be bypassed. Certainly, work is underway to diminish genetic influence.

Colonoscopy in high-risk people should often detect cancers or pre-cancer early leading to better results. For breast cancer family members, medicines like Tamoxifen can decrease the risk of invasive malignancies. Early detection is frequently important. For prostate detection, early diagnosis means the highest cure rates. For this, physical exams, blood testing of PSA or prostatic specific antigens and often ultrasounds or biopsies are crucial.

Cessation of smoking and routine high resolution CT scanning should simultaneously decrease the incidence of lung cancers and increase early detection hopefully also saving lives.

Can we learn from others? Of course. It is the sign of intelligence that we do. As it is said, those who do not learn from history are condemned to repeat it. Let's hope not for those with cancer.