MAURIE MARKMAN, MD
Dr. Markman is director of the Cleveland Clinic Cancer Center and chairman of the Department of Hematology/Medical Oncology at the Cleveland Clinic, and an associate editor of the *Cleveland Clinic Journal of Medicine*.

Calculating cancer risk: It is harder than it seems

The risk for an individual is difficult to define and depends on environmental and genetic factors

This year, more than 1,250,000 Americans will discover they have cancer, and more than 500,000 will die of it. A malignant disease develops in approximately one third of all Americans during their lifetime. More than two thirds of all families are affected.

As the US population ages, the incidence of cancer will increase, as persons are exposed longer to environmental carcinogens such as tobacco smoke and ultraviolet radiation from sunlight. In addition, as deaths from other causes decrease (eg, infections, accidents, strokes, myocardial infarctions), cancer will cause a proportionally larger percentage of deaths.

These alarming facts have led many to wonder what we can do as individuals and as a society to reduce the risk of cancer. However, as we begin to develop strategies to reduce cancer risk, we must understand what the risk really is, how risk-assessment data can be misinterpreted, and how our actions might affect individuals and society.

REASONS FOR CONFUSION

Cancer risk is difficult to assess, although the widespread publicity about cancer risks might make it appear otherwise. A variety of factors make the assessment of cancer risk difficult, especially when we are talking about the risk for a specific individual instead of a population.

Risk factors are poorly understood

Although these figures indicate that malignant diseases cause a major share of disease and death in this country, the risk for a particular person is far more difficult to define, and depends on factors both environmental (such as smoking and asbestos exposure) and genetic. With several notable exceptions, such as cigarette smoking, which directly causes lung cancer, the specific factors and their relative importance in the development of cancer are poorly understood.

Statistics may overstate risk

The lifetime risk of acquiring cancer is much higher than the risk of dying of cancer, at least for younger persons. For example, it has been well publicized that a woman living in the United States has a "1 in 8" chance of acquiring breast cancer during her lifetime. However, only 1 woman in 28 in this country dies of breast cancer.

In addition, as noted above, one of the reasons that the risk of breast cancer (and other cancers) has increased is that persons are living longer. Thus, although 1 in 9 women who live to age 85 will acquire breast cancer, only 1 in 50 do so by age 50.

Several additional examples emphasize the powerful role that age plays in determining cancer risk. A 40-year-old woman has less than a 2% chance of acquiring breast cancer before age 50, and approximately a 4% chance before age 60. In contrast, a 20-year-old woman has only a 0.04% chance of acquiring breast cancer before age 30, and a 0.5% chance before age 40.

New tests may detect clinically insignificant cases

The vastly improved tests available today may have artificially inflated the incidence of some types of cancer. For example, the incidence rates of breast cancer and prostate cancer seem to be increasing alarmingly; yet, many of the extra cases being discovered today consist of small lesions detected by screening mammography or prostate-specific antigen testing, and may never have grown either locally or systemically, and may never have caused any problems. The magnitude of this phenomenon is difficult to quantify.

Problems in interpreting screening tests

With the explosion in knowledge of molecular genetics, we can expect a number of genetic tests to become available to assist in determining relative cancer risk. Although these tests may ultimately be of value in detecting cancer or in deciding if a patient should undergo preventive treatment or even prophylactic surgery (eg, to prevent cancer of the breast or ovary), their role at present remains largely unknown.

A particular concern about such tests is how to interpret positive results. For example, suppose a new test has been approved for commercial use. The test detects a genetic abnormality, present in 0.1% of the population, that almost always leads to a certain type of cancer.

Assume that the test is highly accurate, having a sensitivity and specificity of 99%. This means that the test would correctly identify 99% of persons who have the abnormality, and miss only 1%. Conversely, 99% of persons who do not have the abnormality would have negative test results, and "only" 1% would have false-positive results.

Thus, if 100 000 persons were tested, 100 would actually have the abnormality (0.1% of 100 000). Ninety-nine of these persons would have positive test results (99% true positive), and only one (1% false negative) who had the abnormality would have a false-negative test result.

Unfortunately, 1% of the 99 900 persons who do not have the abnormality would also have positive test results—999 persons. Therefore, 1098 persons would have positive test results, but of these, only 99 would actually have the abnormality. More than 90% of positive test results in this population would be false.

This same concept applies to other screening tests (including serum tumor markers) that attempt to find a relatively uncommon condition in a large population. Unless the specificity of the test is virtually 100%, the chance that a positive result is actually false-positive is considerable.

ZERO CANCER RISK—AT WHAT PRICE?

Public discussion about the risks of acquiring a serious illness or about other societal health issues is often based as much on emotional factors as on the documented importance of the problem. How else, for example, can we explain why politicians and the media focus as much attention on narcotic addiction (which causes fewer than 15 000 deaths per year) as they do on tobacco use (which causes more than 400 000 deaths per year) or alcoholism (more than 90 000 deaths per year)?

Much of the discussion of cancer risk often assumes that we can live in a world in which there are no carcinogens. In fact, it is impossible to completely eliminate the risk of cancer. Efforts to screen all food substances to totally eliminate carcinogens in our diet or remove all potentially cancer-producing substances from the workplace must be weighed against the impact of such efforts on other critically important aspects of our daily lives and societal goals.

For example, the apparent insistence on zero cancer risk recently led a state regulatory body in California to declare tamoxifen a carcinogen, on the basis of a small risk of it causing endometrial cancer, which is highly curable. This bureaucratic ruling was made even though multiple studies have revealed tamoxifen to be highly effective, extremely well tolerated, and capable of significantly prolonging the lives of women with breast cancer. ■

Improved tests may have artificially inflated the incidence of some types of cancer

SUGGESTED READING

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ADDRESS REPRINT REQUESTS to Maurie Markman, MD, Department of Hematology/Medical Oncology, T40, The Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland, OH 44195.