TOXICOLOGICAL EVALUATION

Classifying Substances as Risk Factors for Breast Cancer

Summary

State Health Department researchers reviewed many scientific studies on breast cancer. They then developed a system and classified about 150 substances as to how likely they are to be risk factors for developing breast cancer. This system is being used in the Coram, Mt. Sinai, Port Jefferson Station Follow-up Investigation and will be useful in other investigations as well.

Breast cancer is a disease with many risk factors related to genetics, reproductive history and personal lifestyle. Some substances are also suspected risk factors for breast cancer. State Health Department researchers focused their work on substances identified by agencies such as the National Toxicology Program as having some cancer causing potential.

How Substances Were Classified

State Health Department researchers evaluated evidence from human, laboratory animal and mode-of-action studies to classify the likelihood that a substance may or may not be a risk factor for breast cancer.

- *Human studies (occupational or communty studies).* Good human data can provide direct evidence that exposure to a substance is a risk factor for breast cancer in people. However, breast cancer is a disease with many risk factors that can combine to increase a person's risk in ways that are not fully understood. One difficulty is that this disease is usually detected many years after it begins. A second issue is that people are exposed to many risk factors throughout their lives. As a result, it is almost impossible to identify a single factor that could have increased a person's risk.

- *Laboratory animal studies* can provide conclusive evidence that a substance causes breast cancer in the species being studied. In these studies,

Classification System

State Health Department researchers developed this system and classified substances as risk factors for breast cancer. This system was developed independently of this investigation, but is being used for the first time in the CMP area. The system is based on an evaluation of evidence from existing human, laboratory animal and mode-of-action studies in the literature. More technical details of the classifications and the list of classified substances are found in the *CMP Breast Cancer Follow-up Investigation Working Draft Integration Report, Chapter III.*

Known risk factor for human breast cancer	Sufficient human evidence to establish a cause-and-effect relationship between exposure and breast cancer. Gamma radiation/x-rays was the only substance assigned this classification.
Probable risk factor for human breast cancer	Consistent evidence from human, laboratory animal and mode-of-action studies strongly suggests, but does not demonstrate, a cause-and-effect relationship between exposure and breast cancer in humans. Second hand cigarette smoke is 1 of 21 substances in this class.
Possible risk factor for human breast cancer	The combination of evidence from human, laboratory animal and mode-of-action studies suggests a relationship between exposure to a substance and breast cancer in humans. The pesticide dieldrin is 1 of 63 substances in this class.
Potential to affect breast cancer risk	Evidence is not strong enough for the substance to be classified as a 'Probable' or 'Possible' risk factor for human breast cancer. The pesticide DDT is 1 of 38 substances in this class.
Not classifiable as a risk factor for human breast cancer	Data are nonexistent, inadequate or conflicting about the relationship between exposure to a substance and human breast cancer. The pesticide alachlor is 1 of 25 substances in this class.
Unlikely to be a risk factor for human breast cancer	Consistent negative evidence from animal and mode-of-action studies indicate that exposure to a substance is not likely to cause breast cancer in humans. Lack of evidence does not qualify a substance for this classification. The solvent hexane is one of three substance in this class.

Risk factor— something that has been demonstrated to increase the chance of developing a disease, such as breast cancer. Having or being exposed to risk factor(s) does not necessarily mean that a person will get breast cancer.

Mode-of action— the biological events and processes that can cause a change that can result in a disease, such as cancer.

Exposure— Contact with a substance by breathing, touching or swallowing.

researchers control exposure to other risk factors by creating the same living conditions for an experimental group of animals that is exposed to a substance and a control group of the same species that is not exposed. The health effects for both groups are compared at the end of the experiment. If the experimental group shows more cancer than the control group, scientists conclude that the exposure caused the cancers. However, these experiments provide only indirect evidence of the potential for a substance to cause breast cancer in people because of biological differences between animals and humans.

- *Mode-of-action studies* provide evidence about the biological changes that can start or support the development of breast cancer. When scientists can pinpoint how a substance causes breast cancer in animals, they can then determine whether the same mode-of-action is likely to occur in people.

Uncertainties

Other researchers have developed risk factor classification systems; however their evaluation of substances is not exactly the same as ours. The purpose of the classification, the use of scientific judgement and scientific uncertainty affect how a substance is classified. For the most part, the greater the amount of evidence, the greater the likelihood of scientific agreement about a substance's classification.

State Health Department researchers developed this classification system to generate a list of substances for research and investigation purposes in New York State. Additional substances may be evaluated if evidence exists of an unusual exposure in areas with elevated breast cancer incidence.

A 'weight-of-evidence analysis' was used to classify substances as risk factors for breast cancer. This analysis considers the results of human, animal, and mode-of-action studies before assigning a classification. All three study types are used because each provides information that the others cannot, and collectively, they provide a good scientific foundation for classification.

Studies	Strengths	Limitations
Human	Provide direct evidence to evaluate the relationship between exposure to a substance and breast cancer in people.	Cancer takes a long time to develop and is a disease with many risk factors that can come together to affect a woman's risk in ways that are not fully understood. Because people are exposed to many risk factors throughout their lives, human studies rarely have enough evidence to establish that exposure to a particular substance is a risk factor for breast cancer in people.
Laboratory animal	Provide evidence that exposure to a substance causes breast cancer in the species being studied by controlling exposures to other risk factors.	Biological differences between species and the likelihood that people are exposed to much lower levels of a substance raise questions about the relevance of animal evidence to humans.
Mode-of-action	Provide evidence that the same biological changes that caused breast cancer in animals would also occur in people in response to an exposure.	It is difficult to identify and measure the biological changes that can cause cancer to develop.

About the Coram, Mt. Sinai, Port Jefferson Station Follow-up Investigation

The CMP Follow-up Investigation is being conducted as part of the New York State Cancer Mapping Project, also known as the Cancer Surveillance Improvement Initiative. This investigation follows the Unusual Disease Pattern Protocol, which was developed to conduct investigations in areas where the incidence of a disease is significantly greater than expected. This protocol is being used for the first time during the CMP Investigation to identify unusual environmental and other factors that may help to explain elevated breast cancer incidence in this seven ZIP Code area.

Teams of State Health Department researchers have prepared four evaluations as part of this investigation:

- **Epidemiological evaluation.** A team of epidemiologists has been analyzing breast cancer data, researching what is known about breast cancer and evaluating additional information on women living in this seven ZIP Code area.

- **Toxicological evaluation.** A team of toxicologists has been evaluating substances to characterize the likelihood that they are risk factors for breast cancer.

- **Environmental exposure evaluation.** With input from the communities, a team of environmental scientists evaluated a large number of existing environmental data sets to identify possible exposures to elevated levels of contaminants compared to other areas of the state.

- **Integration evaluation.** These research teams have been working collectively to integrate their results and evaluate health risks associated with identified environmental exposures in terms of their relationship to breast cancer and other non-cancer health effects.

The CMP investigation is ongoing. Researchers are providing their findings to date in the *Coram, Mt. Sinai, Port Jefferson Station Follow-up Investigation Working Draft Integration Report.*

For more information contact
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http://www.health.state.ny.us/nysdoh/cancer/sublevel/follow.htm