EVERYTHING DOESN'T CAUSE CANCER

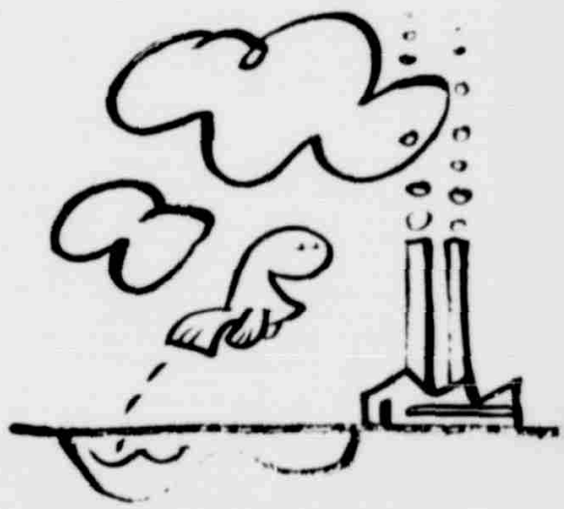


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Cancer is one of the most feared of human diseases. One of every four Americans can expect to get cancer. But the outlook is not hopeless—we can do something about it. This brochure seeks to answer some common questions about the causes and prevention of cancer, and about the laboratory animal tests that identify cancer-causing substances. Methods for testing chemicals and interpreting test results will be emphasized.

Question What causes cancer?

Answer: Cancer is actually many different diseases with many causes. Most human cancers probably are caused in part by environmental factors. Cancer-causing agents, called carcinogens, include certain man-made and natural chemicals which may be found in small quantities in air, water, food and the work place. Cancer-causing agents also include x-rays, sunlight, and certain viruses. Contact with cancer-causing agents may result from individual actions, such as smoking or dietary habits. This brochure deals mainly with chemical carcinogens. It is not true that everything causes cancer, or that the problem is hopeless. Relatively few substances cause cancer. Most chemicals, even most toxic or other dangerous chemicals are not carcinogenic. Susceptibility to carcinogens may vary among individuals.



Certain cancer-causing agents are found in air, water, food and the work place.

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Question: Can cancer be prevented?

Answer: Yes, many cancers could be prevented by reducing our exposure to carcinogens. Some carcinogens can be avoided by personal choice, government regulation, corporate decisions or other societal actions. Reducing human cancer rates by reducing or avoiding exposure to cancer-causing agents is an achievable goal.



Some carcinogens can be avoided by individual choice.

Question: How soon after exposure to a carcinogen does the cancer appear?

Answer: Cancers develop slowly in man, usually appearing 5 to 40 years after exposure to a cancer-causing agent. Cancers of the liver, lung or bladder, for example, may not appear until 30 years after exposure to vinyl chloride, asbestos, or benzidine. This long latent period is one reason why it is so difficult to identify the causes of human cancer.

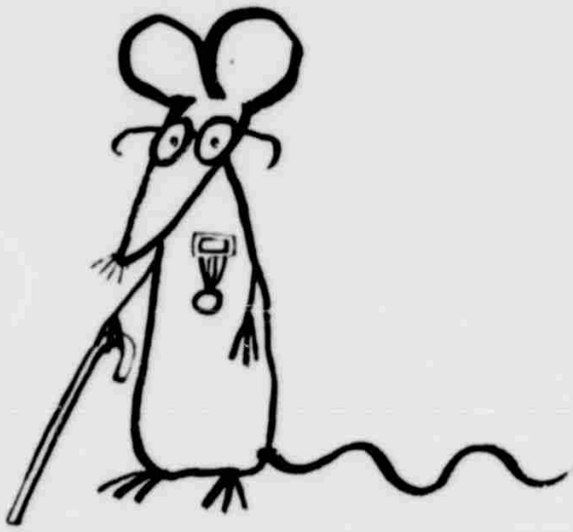


Human cancers usually don't appear until 5 to 40 years after exposure.

Question: How can we identify agents that cause cancer in people?

Answer: It is hard to do so directly because suspected carcinogens are tested on laboratory animals, not people. But direct human exposure to cancer-causing substances has often occurred, nevertheless, and we can study the exposed populations. For example, people who have been exposed to tobacco smoke or asbestos develop after many years a higher frequency of cancer of the lung and other organs than unexposed people.

From such population studies we have identified about 30 agents as human carcinogens.



Mice or rats are used for laboratory tests because generally they are similar to humans in their response to carcinogens.

Question: Aren't there other ways to identify carcinogens, without humans first getting cancer?

Answer: Yes, tests on laboratory animals can identify substances that are likely to be human carcinogens. Mice or rats are most commonly used for such tests because they are small, easily handled, more economical than larger animals, and similar to humans in their response to carcinogens, at least in a general way. Most major forms of human cancer have been reproduced in such animals through exposure to chemical carcinogens. Since their natural lifetime is two to three years, rodents provide information about the cancer-causing potential of test materials more quickly than do longer-lived animals, such as dogs or monkeys. Special strains of mice and rats have been developed to be particularly suitable for carcinogenicity testing.

Question: How well do laboratory animal tests predict whether or not a substance can cause cancer in humans?

Answer: There are two ways to answer that question. Of the approximately 30 agents known to cause cancer in humans, almost all cause cancer in laboratory animals.

Of the several hundred other chemicals that cause cancer in laboratory animals, however, it is not known how many are also human carcinogens. Nevertheless, materials that cause cancer in one mammalian species are usually found to cause cancer in other species. Furthermore, in some instances the risk predicted in advance by tests on rodents were later confirmed by the occurrence of cancer in exposed humans. Chemicals such as diethylstilbestrol (DES), vinyl chloride, and bis(chloromethyl)ether were shown to cause cancer in mice and rats before it was known that people exposed to those chemicals also had increased cancer rates.

We should assume, therefore, that agents that cause cancer in animals are likely to cause cancer in humans. To prevent cancer, we cannot afford to wait for absolute proof of carcinogenicity in humans. Instead, we must heed the warnings provided by laboratory animal experiments and reduce or eliminate human exposure to probable cancer-causing agents.

Question: How are these laboratory animal tests performed?

Answer: In brief, groups of about 50 mice or rats of each sex are exposed to the test substance at different dosages for about two years. Other groups, known as controls, are treated identically, but are not exposed to the test substance. At the end of the experiment, the animals are carefully dissected

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and examined by pathologists (doctors who interpret the changes in body tissue caused by diseases), and the frequency of tumors in the test groups is compared with that of the controls. Carcinogens produce a tumor frequency higher in the exposed animals than in the unexposed control animals. Non-carcinogens, by contrast, do not produce tumors.

Question: We often read about mice or rats being fed dosages much higher than those to which humans would normally be exposed. Are high doses really used, and if so, why?

Answer: Yes, high doses are often used to increase the ability of the tests to detect tumor-causing potential. The public often misunderstands the reasons for high dosage testing, and misinterprets the results.

In the human population, large numbers of people are exposed to low doses of chemicals, but the total impact may not be small at all. For example, a carcinogen might cause one tumor in every 10,000 people exposed to it, which may seem like a needle in a haystack. But exposure of 220 million Americans would result in 22,000 cancers—a public health disaster. We therefore need sensitive tests to detect those agents with the potential to cause only low cancer rates.

We obviously could not identify a carcinogen that causes one cancer in every 10,000 exposed mice by running the test on only 50 mice. To detect such a low cancer rate, we would need tens of thousands of mice, which would cost many millions of dollars per test. Testing more than a few chemicals in such an unwieldy fashion would be prohibitively expensive and time-consuming.

With high dosages, any potential carcinogenic effects are more likely to be detected in small groups of rodents because the cancer rate among the test animals is increased correspondingly. In the above example, a dose 5,000 times higher might cause cancer in 5,000 of every 10,000 mice, or 50 percent of the animals. If 20 or 30 of our test group of 50 mice developed cancers under such conditions, while the control group had only a few cancers, we could properly conclude that the chemical was capable of causing cancer. When high doses do not cause cancer, we also have greater assurance that the chemical is not a carcinogen.

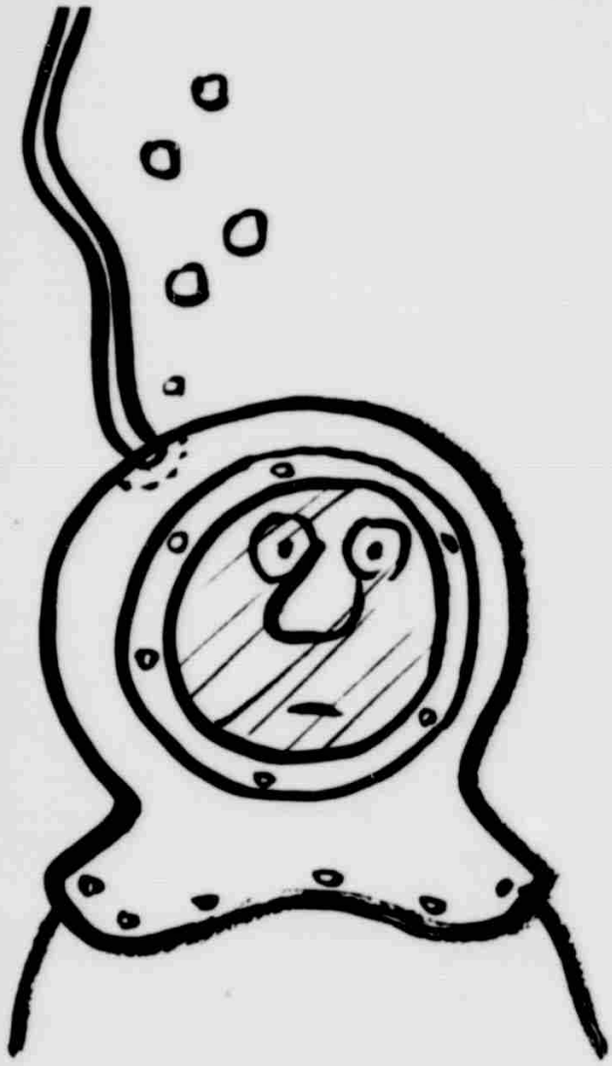
Question: Won't the animals get sick and die if given such high doses?

Answer: No. National Cancer Institute guidelines for testing restrict the doses to levels that will *not* cause significant toxicity or unduly shorten the animals' lives. Because the animals must live long enough for tumors to develop, doses that kill the animals prematurely are not used in tests for carcinogenicity.

Question: Doesn't everything cause cancer if the dose is high enough?

Answer: No. High doses of many chemicals are toxic, but they will not cause tumors. Other forms of toxicity, such as loss of hair or weight, various organ malfunctions, or even death, should not be confused with carcinogenesis.

In one study, 120 pesticides and industrial chemicals were tested at the highest doses the mice could tolerate and survive. These chemicals were not randomly selected, but were chosen because they were suspected of carcinogenicity. Nevertheless, after two years of such treatment, only 11 of these chemicals caused cancer in the test animals.



High doses of many chemicals may be toxic, but not all of them will cause tumors.

Question: Will a carcinogen cause cancer in the same organ when tested in different animal species?

Answer: Often, but not always. Different organs may become cancerous in different species. Thus a chemical that causes cancer of the liver in mice, for example, might cause cancer of the breast in rats and cancer of the bladder in humans. A carcinogen also can cause tumors in several organs in the same species, or even in the same individual.

Question: Why are test animals sometimes exposed to the test chemical in a way different from the way in which humans would be exposed? Hair dyes were *fed* to rats, for example.

Answer: The method of exposure need not be identical, although that is usually preferred. The tests seek to determine the *potential* to cause tumors, and distribution throughout the animal's body is the important part of the test. Hair dyes can enter the circulatory system through either the scalp or digestive tract.

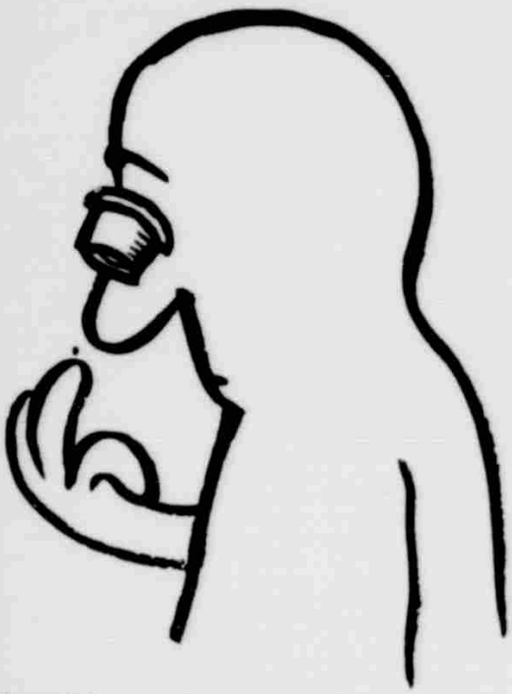
Question: Aren't many of the animal tumors not cancerous?

Answer: Yes, but these tumors also indicate human cancer risk. Noncancerous (benign) tumors often become cancerous. No chemical is known to cause only benign tumors.

Question: How should we interpret the appearance of tumors in one species, such as rats, and the absence of tumors in another species, such as monkeys?

Answer: Positive evidence of tumors in one test is not cancelled by negative evidence, or the absence of tumors, in another test. A substance that is carcinogenic in one strain or species occasionally has little or no effect in another strain or species. Furthermore, not all tests are equally sensitive, and a negative result may mean merely that the effect was missed. Too few animals, too low a dosage, or too short a test period, for example, can lead to a false negative result. A 5-year test on 10 monkeys could fail to detect tumors that would have appeared after 10 to 15 years, or that would have been detectable in 50 monkeys. Any adequately performed positive test in laboratory animals indicates a cancer hazard for man.

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We can't be sure there is any safe level of exposure to carcinogens.

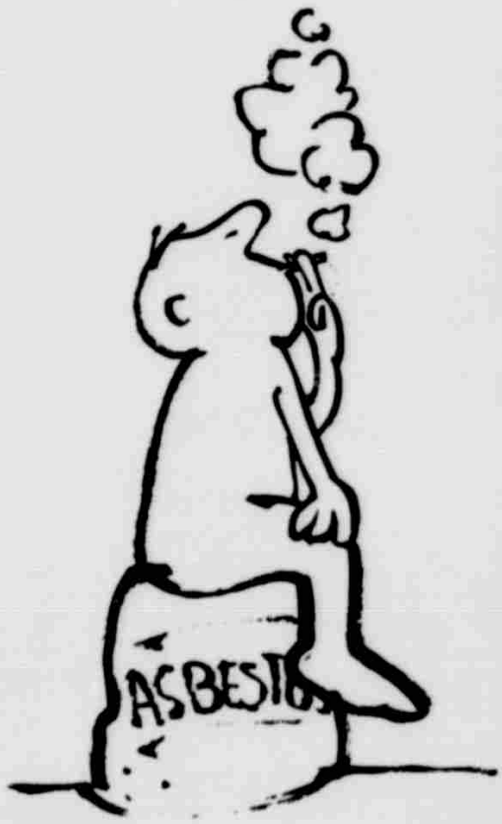
Question: Are there safe levels for human exposure to carcinogens; that is, are there threshold dosages below which we can be sure that no cancer will occur?

Answer: There is no adequate evidence for the existence of a safe threshold for any carcinogen. As far as we know, the frequency of tumor formation declines as the dosage declines, but the risk of carcinogenesis may not disappear until the dosage reaches zero. Although high doses often are used in the tests, we must not assume that only high doses cause cancer. On the contrary, we must assume that low doses will also cause cancer, but at proportionally lower rates.

Human cancers have occurred following very low level exposure. Asbestos brought home on the clothing of asbestos workers, for example, has caused fatal cancers in members of the workers' families.

Question: Can we estimate the magnitude of the human cancer risk from the results of laboratory animal experiments?

Answer: Yes, we can estimate it in various ways, but the estimates usually are crude and we can't always depend on them. Animal tests tell us there is a hazard, but they don't tell us the extent of that hazard. Attempts to quantify the risk can lead to large errors, resulting from different methods of calculating risk, different susceptibilities between laboratory animals and humans, and potential interactions between the agent in question and other chemicals to which man is exposed.



The risk of cancer may be increased when people are exposed to several carcinogens at the same time.

Question: What happens when people are exposed to several carcinogens at the same time?

Answer: The resulting cancer rate may be higher than would be predicted by adding the risks from each carcinogen alone. Cigarette smoking and asbestos exposure, for example, are both carcinogenic, but asbestos workers who smoke are subject to a cancer risk that is far higher than would be expected by adding the risk from smoking to the risk from asbestos.

Question: What is the best way to prevent cancer?

Answer: Individually and collectively, we must make every effort to reduce or eliminate human exposure to carcinogens. This effort applies to agents known to cause cancer in humans, especially tobacco smoke. It also applies to agents that, on the basis of evidence gathered in animal or other experimental studies, are suspected of causing cancer in humans. Because everything does not cause cancer, such an approach to cancer prevention is reasonable and workable.

