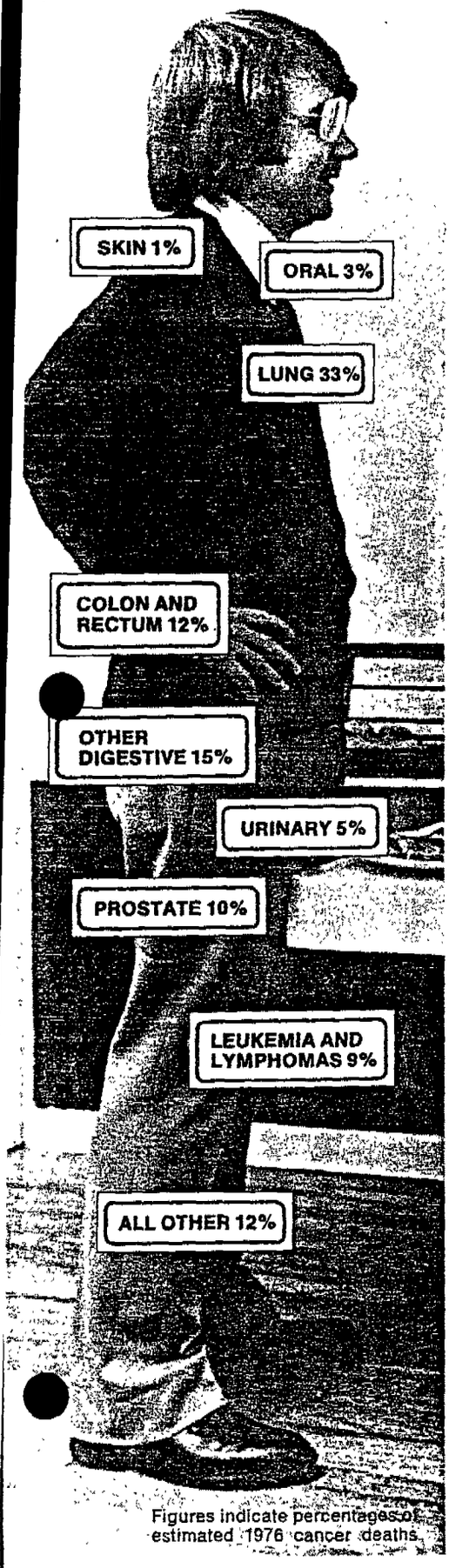


Figures indicate percentages of estimated 1976 cancer deaths

WHAT CAUSES CA

Americans used to think of cancer—when they permitted themselves to think of it at all—as one of those roll-of-the-dice diseases: mysterious, unpredictable and, if your number came up, unavoidably fatal. But recently, they have been learning something new and, in a sense, far more frightening about cancer. In the vast majority of cases, cancer may be a man-made disease.

To judge from newspapers, magazines and television, even the simple acts of eating, drinking, breathing and touching may expose Americans to some possible cause of cancer. Women have been warned not to eat beef liver because it may produce cancer of the vagina. Several of the nation's major sources of water have been found to contain an industrial chemical that causes cancer in laboratory rats. Polyvinyl chloride (PVC), a plastic used in food wrapping, is also under suspicion. Some housewives began to shun bacon and ham after they were told these products contain dangerous chemicals. Perhaps most worrisome of all is the fact that the latest statistics show a cancer-death rise of 3.8 per cent for 1975—though this may be revised when all the figures are in.

Small wonder, then, that many scientific experts have begun to regard the environment—everything we come into contact with—as a far more significant source of cancer than aberrant cellular mutation. Even if the headlines tend sometimes to overstate the case, there seems little doubt that the newest frontier in cancer research has now become the environment itself. Already the World Health Organization estimates that up to 85 per cent of all cancer cases are the direct result of exposure to environmental factors of one kind or another—in many instances almost fatalistically self-inflicted by such habits as overeating, smoking, overdrinking and excessive exposure to sunlight and dangerous chemicals in the factories.

Some scientists, like Dr. Samuel S. Epstein, an environmental toxicologist at Case Western Reserve University Medical School, think that the past two or three decades have witnessed a phenomenon unique in the history of man—"the introduction into the universe of potent chemical agents which are largely untested for adverse public-health effects." Epstein notes that cancer rates have nearly tripled since 1900 (partly because of increased life expectancy, partly because of better diagnostic techniques), and that they have gone up 1 per cent a year since 1933—not to mention the mysterious but still tentative 3.8 per cent increase indicated for 1975. "There is no question," he says, "that cancer is a major epidemic."

Though a number of Epstein's colleagues might choose to state the case less dramatically, few disagree that the environment and what man has done to it loom increasingly as the major sources of the second greatest killer (after heart attacks) in the nation. In coincidental support of this thesis, Academic Press this week will publish a massive, 544-page report entitled "Persons at High Risk of Cancer." Based on a symposium sponsored by the National Cancer Institute and the American Cancer Society, the report offers a sweeping and meticulously documented appraisal of the most recent research on the epidemiology of cancer in man—with special emphasis on the possible roles of diet, drugs, radiation and the workplace.

Already, the concern about the role of the environment in cancer seems to presage a major shift in the application of cancer research funds. Critics charge that the NCI has so far failed to devote an appropriate slice of its $690 million budget to research on cancer control and prevention and on the identification of carcinogens in the environment. They say that NCI researchers are spending an inordinate amount on basic research, including $90 million on a virus program that has yet to uncover a human-cancer virus. The critics charge that even if such a virus is found, it would account for only a small number of cancer cases.

Of the remaining $600 million in the NCI budget, only $45 million will go this year into research on carcinogens. But even this sum represents a new emphasis on cancer prevention. Only $7 million

was devoted to such projects a few years ago. And eventually, NCI plans to spend an additional $50 million on a program to study the role of diet alone in cancer. Last summer, NCI published a "Cancer Atlas" based on a survey of cancer deaths in the 3,056 counties of the contiguous 48 states. "It's generating a lot of ideas of where to look and what to do," says Marvin Schneiderman of NCI. Among the patterns emerging from the cancer map (page 67) were the high rates of bladder cancer in the industrialized Northeast as well as excessive lung and liver cancer rates in smelting-industry communities.

In recent months, the search for cancer-causing substances in the environment has stirred a welter of controversy, involving environmentalists, industry and the scientists themselves. Even the experts disagree somewhat on what substances are hazardous and what ought to be done about them when they are found. Of more than 1,400 chemicals, drugs and pollutants now suspected of causing cancer—mostly on the basis of animal tests—only about 22 are now widely held to be carcinogenic to man.

NCER?

Responsibility for protecting the public from carcinogens is shared by a bureaucratic web of government agencies that includes the Environmental Protection Agency, the National Institute for Occupational Safety and Health, the Occupational Safety and Health Administration and the U.S. Food and Drug Administration. Not surprisingly, their responsibilities not only overlap but are often in direct conflict, with different agencies setting different standards for regulating suspect chemicals.

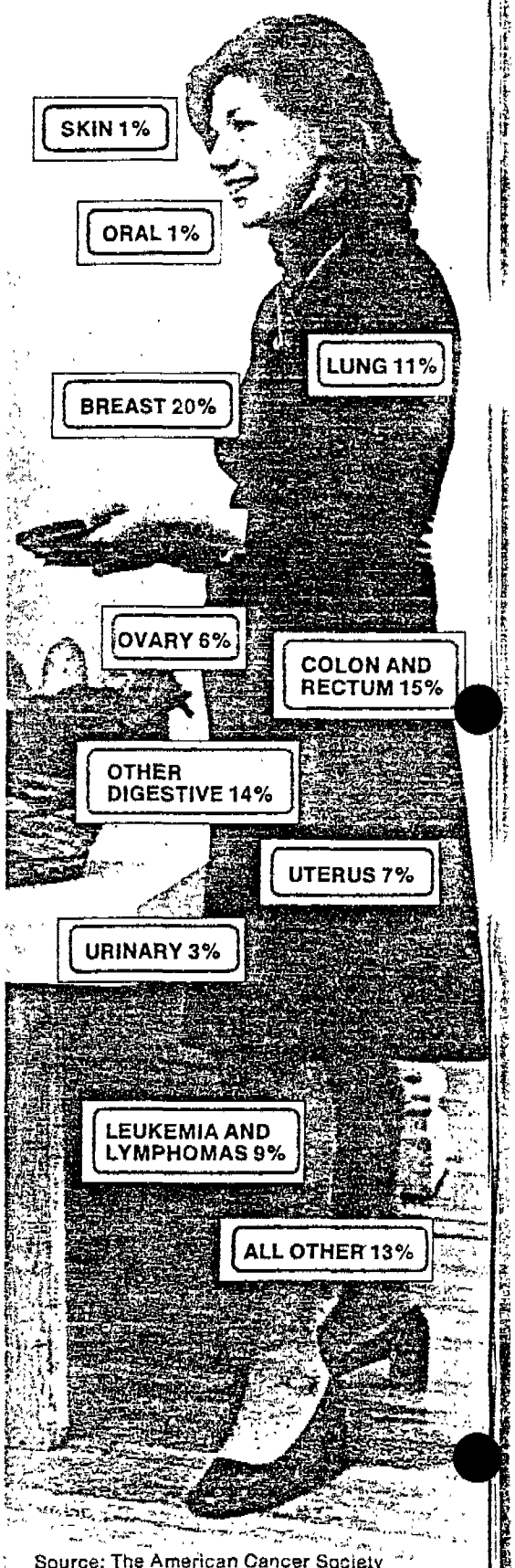
Most experts agree on the need for a law that would mandate testing of all new chemicals and drugs for toxicity—including the tendency to cause cancer—before, not after, they enter the environment. "If you wait till people are hit by the epidemic," says the NCI's Dr. Umberto Saffiotti, "it's too late." Such a bill has lain before Congress for five years, and many critics charge it has been blocked by industry pressure.

The consumerists point to the recent vinyl-chloride episode as a stark example of the failure of the present system to catch a dangerous chemical before it causes trouble. Vinyl chloride is a gas that has been used in ever-increasing amounts in the last 30 years to make polyvinyl chloride, a plastic found in a vast array of items, including food containers and phonograph records. In 1973, Italian reseachers found that VC produced liver tumors in rats. The findings were largely ignored until it was learned that the same kind of tumor—exceedingly rare under ordinary circumstances—had taken the lives of three workers at the B.F. Goodrich plant in Louisville, Ky. Only then were revised standards on exposure put into effect.

For the scientists, there are two major problems in uncovering cancer-causing substances. The first is the long "latent" period—often twenty to 35 years—between the beginning of exposure to a carcinogenic substance and the appearance of malignant disease. In addition, scientists find themselves in disagreement on how big a dose of a substance is enough to trigger cancer. Some researchers point out that almost anything, including sugar and salt, will cause trouble if given in a large enough dose. Most regulations are based on the idea that there is a "threshold" of exposure, below which there is no risk. But many experts insist there is no such thing as a safe level. "Lower concentrations simply mean lower incidence," says Epstein. "There is no threshold."

The second and equally controversial question is whether testing in animals is a reliable indicator of what a substance will do to man. The amount of a substance required to cause cancer in an animal may not realistically reflect the amount that humans can safely be exposed to. But toxicologist Epstein insists that animal results are applicable to man. "Information in tests from well-designed and valid animal systems," he says, "constitutes very strong evidence for a cancer hazard in humans."

Some manufacturers have been suspected of hiding or falsifying test results indicating a cancer hazard. Last week, NEWSWEEK learned, the EPA and the Department of Health, Education and Welfare were thinking of taking criminal action against several corporations and commercial testing labs for just such fraud. The agencies are also planning to look into conflict-of-interest charges in-



Source: The American Cancer Society

Photos by Frances McLaughlin-Gill

volving scientists who act as paid advisers to regulatory agencies while getting consultant fees from private companies.

Workers who have been exposed to carcinogens in their jobs are often amazingly philosophical about the life-threatening risk they are taking. Charles Russell of New York has been inhaling asbestos fibers for 28 years as an insulation worker. Now, he turns up regularly at his union headquarters for lung-cancer checkups conducted by Dr. Irving Selikoff of New York's Mount Sinai Hospital, who was among the first to show that asbestos workers exhibit a high propensity for the disease. "It's a bad risk," says Russell, who is healthy so far, "but where are you going to find work? I'm taking home $230 a week, so what can you do?"

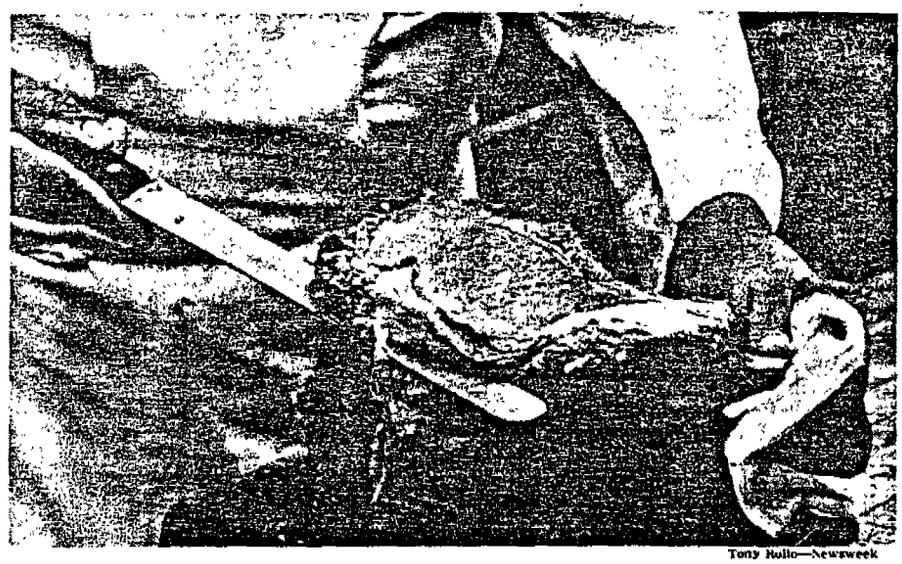
Clearly, the environment is never going to be entirely free of carcinogens, and the government, researchers and consumers have to make practical choices about the risks they are willing to take. "Before eliminating pesticides like DDT," says E. Cuyler Hammond, chief of epidemiology for the American Cancer Society, "you must carefully consider what it might mean for the health and nutrition of much of the world."

The outcry that follows each successive new disclosure of a possible carcinogen on the dinner table or in the work shop tends to obscure the fact that 60 million Americans continue to expose themselves to tobacco—the least disputed carcinogen of all. Moreover, many experts believe the problem has been exploited to an unconscionable degree by some overzealous consumers, organic-food promoters and the news media. "American cancerophobia," noted a recent editorial in the prestigious New England Journal of Medicine, "is a disease as serious to society as cancer is to the individual."

The truth is that cancer is not one disease, but at least 100 separate diseases involving a derangement in the life of the body's cells. Only by studying the epidemiology of cancer in humans on a vast scale can the effect of life-style on the disease be determined. Following are some of the most important and promising clues on the questions of environment and cancer, taken from the just-published "Persons at High Risk of Cancer" and interviews by NEWSWEEK reporters:

1. FOOD AND DRINK

Foods and food additives may contribute to cancer through complex chemical interactions that have only recently come under scrutiny. A case in point is the controversy over sodium nitrate and sodium nitrite. They are naturally present in many foods and some water supplies, and are added to bacon, ham and smoked foods to enhance their color and inhibit the growth of the deadly bacteria that cause botulism. Although not carcinogenic by themselves, they combine with amines (chemical compounds derived from ammonia) found in the body to form nitrosamines. And nitrosamines are highly potent carcinogens in animals.



Tony Rollo—Newsweek

Food: In an affluent society, the better fed may be worse off

Robert R. McElroy—Newsweek

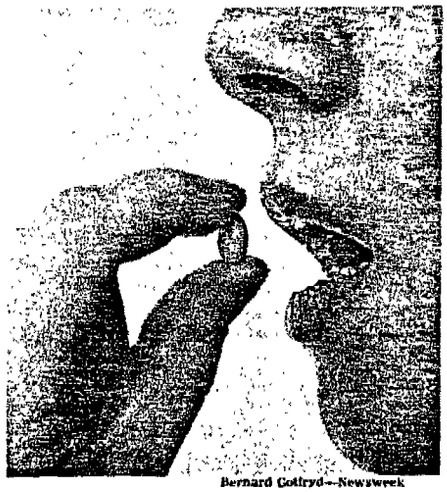
Factories: Asbestos plants are high on the risk list

Several epidemiologists have tied nitrates in smoked fish to the high incidence of stomach cancer among the Japanese. Yet there is no evidence that nitrosamines from nitrates and nitrites in the American diet are a threat. For one thing, these substances volatilize during cooking, notes Dr. Philippe Shubik, director of the Eppley Institute for Research in Cancer at the University of Nebraska, so exposure to nitrosamine after eating cured meat would be low. Moreover, nitrites are abundant in saliva. "Every day," notes Dr. Thomas Jukes of the University of California, "we swallow as much nitrite as found in a pound of bacon." Interestingly, vitamin C can block formation of nitrosamines—at least in the test tube. "The same individuals who put themselves at risk by eating bacon every morning," writes Dr. John W. Berg of the University of Iowa, "may be protected by preceding the bacon with orange juice."

The case against artificial sweeteners is also weak. Some studies made after cyclamates were removed from the market have failed to confirm that cyclamates cause bladder cancer in animals, and the FDA is seriously considering lifting its ban. Although saccharin has been found to cause cancer when implanted directly into the bladder, it is far from clear that it is hazardous if consumed in the diet. Significantly, diabetics have been consuming saccharin for years, yet there is no sign that they have a higher than normal cancer risk.

Of greater concern is the link between the fatty diet of affluent countries and the risk of two of the most prevalent malignant diseases—cancer of the bowel and breast. Bowel cancer is common in the U.S., but uncommon in Japan, where fish is a staple. However, among Japanese migrating to the U.S. and their children, the colon-cancer risk approaches the U.S. level, presumably because of a change in dietary habits. Beef is a likely suspect. The Scots, who consume 20 per cent more beef than their English neighbors, have one of the world's highest bowel-cancer rates.

Cancer of the breast, as well as the prostate, ovary and uterus, is prevalent in most Western countries and may also be related to heavy fat intake. Breast cancer has been linked to overnutrition in women, and fats have been found to promote breast cancer in mice.



Bernard Gotfryd—Newsweek

Drugs: Dangers sometimes outweigh gains

Hormones are known to play a part in breast cancer and the current suspicion is that fats may overstimulate hormone production or disrupt normal hormone balance.

Too much liquor is related to the development of cancers of the mouth, throat, esophagus, larynx and liver. But the risk is greatest among heavy drinkers who also smoke, giving rise to the belief that alcohol is a co-carcinogen, acting in conjunction with tobacco carcinogens. Among men who drink more than an ounce and a half of liquor a day, the mortality from oral cancer is two to six times greater than it is for teetotalers, depending, in direct proportion, on the amount they smoke. For heavy drinkers and smokers, the risk is up to fifteen times higher than for those who neither drink nor smoke.

London Daily Express

Radiation: Overexposure to the sun may cause skin cancer

2. DRUGS

Many epidemiologists are more concerned about the cancer potential posed by drugs than they are about food additives, because drugs are taken in relatively large doses. A certain cancer risk, in some cases, may be outweighed by the seriousness of the disorder the drug is designed to treat, so physicians must balance the benefit against the risk. One of the most disturbing links between a drug and cancer was the discovery in 1971 that the daughters of women who took the synthetic estrogen diethylstilbestrol (DES) in early pregnancy were susceptible to an often fatal vaginal cancer (box, page 66).

DES was given to thousands of women after World War II on the theory that it would prevent miscarriage. Much later, Dr. Arthur L. Herbst and his colleagues at Massachusetts General Hospital encountered seven young women with a vaginal adenocarcinoma, a disease that is not only rare, but had almost never before been found in a woman under the age of 50. Checking the medical histories, the doctors found that all their patients' mothers had used DES in pregnancy. Since that initial report, more than 250 similar cases have been documented.

More recently, several studies have suggested that the use of estrogens by middle-aged women to alleviate symptoms of the menopause increases their risk of uterine cancer. Researchers at the University of Washington reported that the risk of cancer was nearly five times higher among women who took the hormones than among those who didn't.

A major unresolved question is whether the birth-control pill—taken by 10 million U.S. women—also poses a cancer risk. In experimental animals, estrogens, which are a constituent of the pills, have

CANCER AND THE ENVIRONMENT: TEN TOP SUSPECTS

SUBSTANCES	WHERE FOUND	CANCERS THEY MAY CAUSE
ARSENIC	Mining and smelting industries	Skin, lung, liver
ASBESTOS	Brake linings, construction sites, insulations, powerhouses	Lung, pleura, peritoneum
BENZENE	Solvents, oil refineries, insecticides	Bone marrow
BENZIDINE	Rubber making, dyestuffs	Bladder
COAL-COMBUSTION PRODUCTS	Steel mills, petrochemical industry, asphalt, coal tar	Lung, bladder, scrotum
NICKEL COMPOUNDS	Metal industry, alloys	Lung, nasal sinuses
RADIATION	Ultraviolet rays from the sun, medical therapy	Bone marrow, skin, thyroid
SYNTHETIC ESTROGENS	Drugs	Vagina, cervix, uterus
TOBACCO SMOKE	Cigarettes, pipes, cigars	Lung, bladder, mouth, esophagus, pharynx, larynx
VINYL CHLORIDE	Plastics industry	Liver, brain

Fenga & Freyer

Watch list: In a world full of possible carcinogens, some substances have been identified as particularly dangerous

Photos by Ted Lau

Mrs. Malloy and Marilyn: A drug with a deadly delayed reaction

DAUGHTERS OF DES

For Grace Malloy, childbearing did not come easily. Although her first daughter was born in 1946 without complications, a subsequent pregnancy ended in miscarriage. When during her next pregnancy she also showed signs of miscarrying, her doctor prescribed diethylstilbestrol (DES), a synthetic estrogen widely used in such cases at the time. A second daughter, Patti, was delivered in 1951. After yet another miscarriage, Mrs. Malloy became pregnant a fifth time and was again given DES. Another daughter, Marilyn, was born in 1956.

It was not until Patti and Marilyn were 19 and 14 that Grace Malloy read a newspaper report linking DES to a rare but deadly form of vaginal cancer in young women whose mothers had taken the hormone during pregnancy. Alarmed, Mrs. Malloy asked her doctor if there was anything to this "scare." "You bet your life there is," he replied. "You'd better get those girls in for an examination right away." The result was bad news: Marilyn had vaginal cancer.

Malignancy: In an operation lasting more than twelve hours, Marilyn's vagina and nearby lymph glands were removed; an artificial vagina was constructed using skin grafts from her legs. The doctors were hopeful that they had excised the entire malignancy, but a year later they discovered that the cancer had spread to one lung, the esophagus and the lining of the heart. Following another operation, Marilyn recovered sufficiently to resume her passion—horseback riding.

A short time later Marilyn's condition worsened. She lost her appetite, suffered from nausea and severe headaches. Tests revealed that the cancer had reached her pituitary gland, and Marilyn underwent a grueling six-week regimen of "whole head" radiation. When all her hair fell out as a result, she still refused to give in to self-pity and kept up an active social life, wearing a bright scarf over her head. But at night Mrs. Malloy could hear her daughter moaning in pain with the cancer that was continuing its lethal spread through her arms, legs, spine and brain. Soon she was blind and confined to a wheelchair. Marilyn died on May 26, 1974, two weeks before her high-school class's graduation.

Guilt: Today, sitting in her elegant, sun-filled La Jolla, Calif., living room, Grace Malloy tells Marilyn's story with self-control. She does not savor pathos. Nor does she feel any personal guilt over her daughter's tragic death. "I had no way of knowing what those pills would do," she says. "Thousands of women took them, but we all did it in the best of faith, because our doctors prescribed them."

Nonetheless, Grace Malloy is not without bitterness about what happened to her family—and what still may lie ahead. Her older daughter, Patti, now 25, has been diagnosed as having vaginal adenosis, a lesion that appears benign but could be the precursor of cancer. In spite of long-standing reservations, Patti recently decided to get married, and her doctors claim her prospects for a healthy future are good. But there is no guarantee; for the time being, Patti can only wait—like thousands of other young women with the same history—and pray that the killer that claimed her sister may pass her by.

—JEAN SELIGMANN with LAWRENCE SHOOK in La Jolla, Calif.

been shown to cause breast cancer. One recent study suggested that the risk of breast cancer was increased for women who took the Pill before having their first child and for those with a history of benign breast tumors. But at least three other surveys failed to show a connection between oral contraceptives and breast cancer.

Drugs used to prevent rejection of organ transplants by suppressing the immune response have also been found to cause cancer. Among more than 6,000 kidney-transplant recipients, the risk of lymphatic cancer was found to be 35 times greater than normal. Of concern to some experts is the fact that one such drug, methotrexate, is being prescribed for the treatment of severe psoriasis.

3. RADIATION

There is no question that X-rays and similar forms of radiation can cause leukemia and other forms of cancer if received in high doses. Survivors of the Hiroshima and Nagasaki atomic blasts have shown a significantly higher than average incidence of leukemia, as well as of cancers of the breast, bowel and brain. Recently, it has been found that those treated with radiation in childhood for tonsilitis, enlarged thymus glands and other conditions during the 1940s and 1950s have an increased risk of thyroid cancers. What is not clear, is how much risk there may be from exposure to conventional diagnostic X-rays.

According to Lorne Houten of Roswell Park Memorial Institute, Buffalo, N.Y., the amount of radiation from a single abdominal X-ray increases the risk of leukemia. One rad (the standard unit of dosage) of radiation, says Houten, ages the cells it strikes by one year. Thus, a 50-year-old man who has received 10 rads has the susceptibility of nonlymphatic leukemia—a form of the disease that strikes adults—of a 60-year-old. In addition, irradiation of men and women during their reproductive years increases the likelihood that their offspring will develop leukemia. On the basis of these observations, Houten thinks that no one should undergo routine screening X-rays—including mammography to detect breast cancer—below the age of 50. An exception, in his view, would be a woman with a family history of breast cancer.

But other cancer experts disagree. Dr. Luther Brady of Hahnemann Medical College, for one, disputes Houten's correlation between diagnostic X-rays and leukemia. "I don't think anybody has confirmed that 1 rad increases the risk of leukemia," he says. E. Cuyler Hammond also disagrees with Houten's feeling about mammography. "The benefit exceeds the risk," says Hammond, "if it is a risk at all."

Ultraviolet radiation from the sun increases the risk of skin cancer. A committee of the National Academy of Sciences recently estimated that among white persons living along the 40th parallel

(Philadelphia, for example), 40 per cent of melanomas and 80 per cent of other types of skin cancer could be attributed to ultraviolet rays. Fortunately, most skin cancer is slow-growing and has a low mortality. Melanoma, however, is one of the deadliest cancers. Indicative of the role of sunlight in this type of cancer is the fact that the mortality from melanoma is 75 per cent higher in the band of states running from Louisiana to South Carolina than in the northern latitudes from Washington to Minnesota.

4. THE WORKPLACE

The list of substances that threaten Americans in the workplace is long and growing longer. Chromates, which are used in paints, pose a hazard of lung cancer. Rubber workers have an increased risk of leukemia from exposure to benzene. Lung cancer and lymphoma have been found to occur at a high rate among workers exposed to inorganic arsenic, which is a basic material in more than 40 jobs from tinting windshields to spraying roses. Like vinyl chloride, arsenic has also been linked to liver cancer. For 80 years, benzidine [used in dye making] has been known to cause bladder cancer. It has been withdrawn in Great Britain, the Soviet Union and several other countries, but is still widely used in the U.S.

Many of the occupational carcinogens their work in combination with other noxious agents. Mount Sinai Hospital's Irving Selikoff and the ACS's Hammond found that asbestos workers develop a higher than normal rate of lung cancer only if they also smoke (although nonsmokers among them have high risk of colon cancer and an abdominal and chest tumor called mesothelioma). The incidence of lung cancer among asbestos workers, in fact, was eight times what it was for smokers in other industries and a startling 92 times the incidence found in nonsmokers.

Of considerable concern among the experts is the risk that hazardous substances pose for persons living near plants or for the families of workers. Epidemiologists in South Africa and England have found mesothelioma in a number of men and women who had never been inside an asbestos plant, including a few who had simply lived in the households of asbestos workers. In the U.S., people living in communities where there are copper-smelting facilities have a higher than expected average of lung cancer. Some experts are beginning to uncover what seem to be community-wide effects from vinyl chloride. In three Ohio towns where vinyl chloride was used in industry, researchers have found a mysterious number of deaths from cancers of the central nervous system in the adult population—as well as neural malformations in children.

Most experts admit that the task of detecting and ultimately controlling all the potential cancer-causing threats in the environment is, practically speaking, impossible. But they do insist that if there were legal regulations to screen dangerous chemicals before they reached the workplace—or the home—the risks could be greatly reduced. "Dangerous chemicals," says Warren Muir of the White House Council on Environmental Quality, "can be controlled."

Beyond such enforcement measures, the real task of lowering the incidence of cancers induced by the American lifestyle is essentially up to ordinary citizens—and here the outlook for constructive action does not seem so bright. For despite all the warnings, the majority of Americans continue to indulge themselves in the potentially harmful pleasures that their opulent society provides, and so far they are apparently content to take the perils along with the pleasures. "Right now we've decided that this is the way we want to live and die," says Dr. David Baltimore, who won a 1975 Nobel Prize for basic cancer research. "And that's the real challenge in American health today."

—MATT CLARK with MARIANA GOSNELL and DAN SHAPIRO in New York, JAMES BISHOP JR. and EVERT CLARK in Washington and bureau reports