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OncoLog

Pregnancy and Cancer Treatment Often Are Not Mutually Exclusive

by David Galloway

Pregnancy, with its combination of physical and hormonal changes, is hard enough on a woman's body. The last thing a mother-to-be needs is the added complication of cancer. Unfortunately, about one in every 1,000 pregnancies does coincide with cancer. Often, these women are advised to terminate their pregnancies, but many women are able to undergo effective treatment for their cancer and deliver a healthy baby.

"We continue to see patients, and the first thing that has been recommended to them is that they terminate the pregnancy. And for some people, that may be their choice, and that may be what they want to do," said Richard L. Theriault, D.O., a professor in the Department of Breast Medical Oncology at The University of Texas M. D. Anderson Cancer Center.

"Depending on the stage of their cancer and their medical health, ending the pregnancy may be appropriate," added Karin M.E.H. Gwyn, M.D., an assistant professor in the Department

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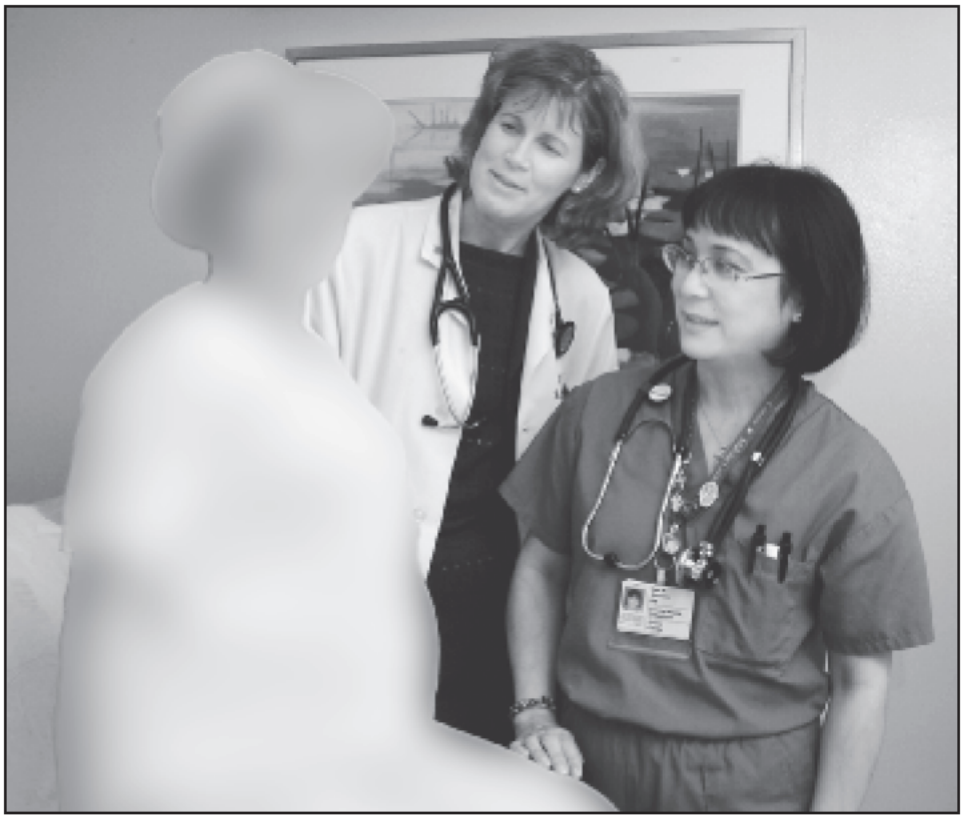

Patient [redacted] *(left), who was treated for breast cancer while pregnant and delivered a healthy baby boy on January 6, 2004, consults a few weeks before the delivery with* **Dr. Karin M.E.H. Gwyn** *(center), an assistant professor in the departments of Breast Medical Oncology and Epidemiology, and* **Lea M. Stavena**, *R.N., a nurse in the Nellie B. Connally Breast Center.*

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Pregnancy and Cancer Treatment Often Are Not Mutually Exclusive

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of Breast Medical Oncology and the Department of Epidemiology, "but it is not always necessary." Pregnant women can undergo biopsies and even be treated for cancer with chemotherapy.

The cancer most commonly diagnosed during pregnancy is breast cancer, followed by cervical cancer, then lymphoma and thyroid cancer. Less common are leukemia and melanoma. With the exception of most cases of cervical cancer, pregnancy and cancer treatment are not mutually exclusive.

"In cervical cancer, the standard treatment is surgery [radical hysterectomy] and radiation," Dr. Theriault said. "The issue is that the fetus is going to die from the treatment, except in unusual circumstances where the cancer is diagnosed early through a Pap smear and you are able to remove all the cancerous tissue with a cervical core biopsy and maintain the pregnancy and delivery."

The outlook is much better for patients with breast cancer. Drs. Theriault and Gwyn work with women who have been diagnosed with breast cancer during pregnancy. Since 1989, their group has treated more than 50 such women. Most of the cancers they see are already at an advanced stage at the time of diagnosis, in part because both patients and physicians tend to dismiss breast lumps during pregnancy as changes related to the pregnancy. "They put it down to mastitis, blocked milk duct, some other reason," Dr. Theriault said. He also cites a common fallacy that even if there is an anomaly in the breast, nothing can be done about it while the woman is pregnant. Some physicians will not even do a biopsy until after delivery, Dr. Gwyn said, further delaying diagnosis and treatment. Both recommend that all pregnant women be given a thorough clinical breast examination on their first visit to the obstetrician, when the women are still early in their pregnancies and the breasts have not yet become engorged.

The incidence of breast cancer concurrent with pregnancy is expected to increase as more women delay childbearing and as mammographic screening increases. The National Cancer Institute's Surveillance, Epidemiology, and End Results Program's Cancer Statistics Review found that women who have their first full-term pregnancy after age 30 have a two to three times higher risk of breast cancer than women who have their first pregnancy before age 20. Among the women in the M. D. Anderson cohort, the median age is 33, and the oldest woman among the patients is 42. As a result, Dr. Theriault urges increased suspicion of any changes in the breasts of pregnant women in their 30s or 40s.

Since 1989, more than 50 pregnant women with breast cancer have been treated at M. D. Anderson. **Dr. Richard L. Theriault**, *a professor in the Department of Breast Medical Oncology, displays a photo of a healthy baby born to one of these women.*

When an anomaly is found, Dr. Gwyn recommends that obstetricians seek the help of cancer specialists rather than keep the burden of diagnosis on themselves. Accurately reading a mammogram or an ultrasound of a pregnant woman's breast is difficult and requires experience, as does interpreting the results of a biopsy from a lactating breast.

If a pregnant woman is found to have breast cancer, chances are it will be an aggressive cancer. That unfortunate fact is not related directly to the pregnancy but rather to the age of the patients. "The tumors occurring in pregnant women are no different than the tumors occurring in other young women," said Lavinia P. Middleton, M.D., an assistant professor in the Department of Pathology, "but breast cancer in young women is a histologically aggressive disease, so it's more the age of the patient than her pregnancy status that affects the tumor's growth and prognostic markers."

If the tumor is found early, though, that histological aggressiveness can be to the patient's advantage. "Tumors that have aggressive histological features, it sounds like they are bad tumors, something that you don't want to have," Dr. Middleton said. "But actually they may respond better to chemotherapy because of the rapid turnover of the tumor cells."

The preferred treatment for a woman diagnosed with locally advanced or node-positive breast cancer during pregnancy is chemotherapy after the first trimester, followed by surgery, usually after childbirth. Radiation therapy is typically not used until after delivery in pregnant patients. The chemotherapy administered is a standard breast cancer treatment combination of 5-fluorouracil, doxorubicin (Adriamycin), and cyclophosphamide (FAC). "We give it the way that we would give it to a nonpregnant woman, and we use the same dosages that we would use for a nonpregnant woman," Dr. Gwyn said. Taxanes are not approved for use in pregnant women, so patients with node-positive disease are given FAC during pregnancy and a taxane after delivery.

"Depending on the stage of [the patient's] cancer and [her] medical health, ending the pregnancy may be appropriate, but it is not always necessary."

– Karin M.E.H. Gwyn, M.D., assistant professor, Departments of Breast Medical Oncology and Epidemiology

The fear that chemotherapy will have adverse effects on the unborn child has been somewhat relieved by a follow-up survey among the patients in the M. D. Anderson cohort. Of the 27 children included in a survey of their parents or guardians, all but three were reported healthy and developing normally. The only exceptions were one child with Down's syndrome, which Dr. Gwyn said has nothing to do with chemotherapy, and two children with attention deficit disorder, which is not uncommon. One question that remains unanswered is whether the fertility of these children will be affected, because the oldest child from this study is only 13 years old. However, the researchers are encouraged by the results of a study of pregnant patients with lymphoma who were treated with chemotherapy. Their children have been monitored for more than 18 years, and some of them have already demonstrated fertility.

With the proper attention and a high index of suspicion, more of these aggressive breast tumors can be caught early. "Even with those negative prognostic attributes and characteristics, these tumors still can be treated successfully," Dr. Middleton said. "And the patients can go on to lead productive lives." ●

FOR MORE INFORMATION, *contact Dr. Theriault or Dr. Gwyn at (713) 792-2817 or Dr. Middleton at (713) 745-0128.*

Studies of the Viral Origins of Some Cancers Lead to New Prevention, Treatment Strategies

by Katie Prout Matias

Viruses are nefarious: They not only make people sick with deadly diseases such as AIDS and smallpox but also, by wreaking havoc on normal cellular functions, set the machine of carcinogenesis in motion. Like other viruses, cancer-causing viruses infiltrate cells and use their DNA-synthesizing proteins and mechanisms to replicate. If the cell-cycle control is disrupted in the process and the infected cell grows unchecked, the initial stages of cancer have begun.

Infectious agents contribute to up to 30% of cancer cases worldwide. The four cancers most often caused by infection—both bacterial and viral—are cervical cancer, liver cancer, Kaposi's sarcoma, and gastric cancer. In most cases of infection with a cancer-causing agent, cancer does not develop; thus, infection is only one component of a multifactorial process that may lead to cancer.

"The goal of the virus is not to make cancer. It is really to keep the cell alive so the virus can propagate," said Felipe Samaniego, M.D., an assistant professor in the Department of Lymphoma at The University of Texas M. D. Anderson Cancer Center. "The virus produces proteins that prevent cell death, or apoptosis, and it has multiple genes meant to keep the cell alive. If a cell accumulates damage and has a virus that does not allow the cell to fix itself, the cell has the tendency to undergo

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Dr. Felipe Samaniego *(right), an assistant professor in the Department of Lymphoma, speaks with patient* [redacted] *(center) and* **Amira Pugh**, *B.S.N., a nurse in the Lymphoma and Myeloma Center.* [redacted] *is part of a study in which non-Hodgkin's lymphoma tumors are being screened for the presence of simian virus 40 DNA sequences.*

Studies of Viral Origins of Cancer

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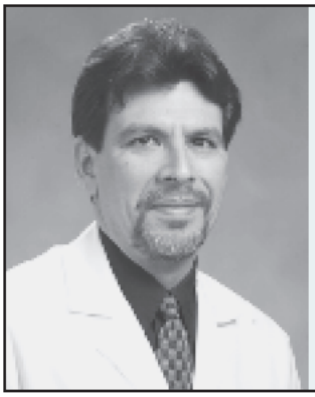
transformation. Once it becomes a transformed cell, the virus is dispensable; the cancer has already taken over and decided what it wants to do."

Researchers have spent decades trying to uncover which viruses contribute to which cancers and how infections can be prevented. While teams of investigators in several countries are working to develop vaccines, the list of suspected carcinogenic viruses continues to grow.



"[Cervical cancer] is the only cancer in which a single cause has been identified… to have the cancer, you have to have the virus."

– Guillermo Tortolero-Luna, M.D., associate professor, Department of Gynecologic Oncology

Cervical cancer

The clearest culprit in viral oncogenesis is the human papillomavirus (HPV), which is present in 100% of cervical cancers. "This is the only cancer in which a single cause has been identified," said Guillermo Tortolero-Luna, M.D., an associate professor in the Department of Gynecologic Oncology. "Cervical cancer is the only one that, in order to have the cancer, you have to have the virus."

More than 100 viruses are classified as HPV, and 40 of these are linked to cancers of the cervix, anus, vulva, vagina, penis, oropharynx, mouth, and skin. All HPV variants are spread primarily through sexual contact. The high-risk strains—including HPV-16, HPV-18, HPV-31, and HPV-45—are also the most common strains, accounting for 80% of infections, said Dr. Tortolero-Luna.

Worldwide, HPV is the most prevalent sexually transmitted disease, and cervical cancer is the second most common cancer among women. Sexually active women have a 75% lifetime risk of contracting HPV; 5.5 million women contract HPV each year. According to Dr. Tortolero-Luna, 80% of women infected with HPV will clear the virus from their bodies within 12 to 18 months. For every 1 million women infected, 100,000 will have precancerous changes in their cervical tissue. Of these, carcinoma in situ will develop in about 8,000, and invasive cancer will develop in about 1,600.

Because so few cases of infection lead to cancer, researchers believe that host, environmental, and viral cofactors are necessary for carcinogenesis. Known cofactors include immunocompromise, smoking, oral contraceptives, childbearing, other sexually transmitted diseases, and a persistent HPV infection, said Dr. Tortolero-Luna.

In developed countries, up to 80% of cervical cancers are prevented with screening and treatment. Cervical cancer is most widespread in underdeveloped regions in South America and parts of Asia and Africa. "The problem more than anything is access: access to screening and adequate treatment," Dr. Tortolero-Luna said. "What we see is that cervical cancer is basically a disease of the underserved populations." A vaccine preventing HPV infection would be most helpful to these women.

"Right now, a lot of HPV research is moving into the prevention arena," said Dr. Tortolero-Luna. "We will see less and less research focusing on cervical cancer and more research focusing on the virus itself." At M. D. Anderson, Dr. Tortolero-Luna and others have been studying women who are infected with high-risk strains of HPV and measuring their immune system responses to the virus at the time of treatment and six months after treatment to determine whether immune response is a predictor of cervical dysplasia. The purpose is to identify peptides in the immune response that could be used to make a vaccine.

All over the world, clinical trials of potential HPV vaccines are under way. Many of the vaccines are "cocktails," or combination treatments, for the most prevalent strains of HPV. Some vaccines work by inducing an immune reaction to HPV's E6 and E7 proteins, which attach themselves to the tumor suppressor genes p53 and Rb and block their control of cell division, thus allowing cells to divide at will. "The vaccines have been shown to be effective already," said Dr. Tortolero-Luna. "Preliminary data have shown that patients who are infected before vaccination have a higher rate of clearance of the infection, and patients who have not been infected have lower rates of infection."

Liver cancer

Another cancer strongly associated with viral infection is liver cancer. Together, cervical and liver cancers account for 80% of all virus-related cancers. The main risk factor for hepatocellular carcinoma is infection with either the hepatitis B virus (HBV) or the hepatitis C virus (HCV). Worldwide, 300 million people in underdeveloped countries are thought to carry HBV, which is often transmitted from mother to child. In the United States, an estimated 1.25 million people are infected with HBV. Approximately 170 million people worldwide and 3.9 million Americans are infected with HCV.

"In the case of hepatitis B, the virus appears to be both directly and indirectly carcinogenic. Clearly, viral DNA has been integrated into cells in about 95% of hepatitis B–related hepatocellular carcinomas, but there may be indirect activation of a variety of genes that cause mutation or activation of the pathways that could lead to carcinoma," said Robert Bresalier, M.D., a professor

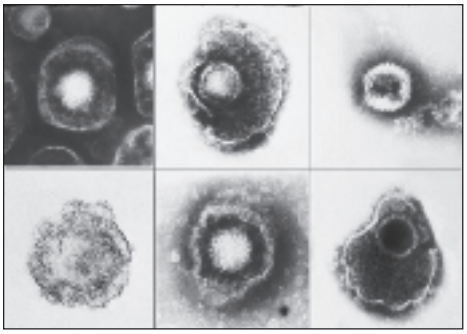
in the Department of Gastrointestinal Medicine and Nutrition.

Malignancy, which can take 30 to 40 years to develop, may be related to an inflammatory process caused by HBV. "Chronic inflammation eventually can lead to carcinoma," said Dr. Bresalier. "Viruses play a major role in the development of hepatocellular carcinoma through a long-term process that involves chronic infection, damage to the liver, cirrhosis, and then, eventually, cancer. That is true classically for hepatitis B but probably also for hepatitis C."

A vaccine for HBV was developed in the 1980s, but researchers have not yet developed one for HCV, which is becoming an epidemic, according to Dr. Bresalier. He is nonetheless confident that a vaccine for HCV will one day be available. In the meantime, physicians at M. D. Anderson treat infected patients with interferon and antiviral medications, and Dr. Bresalier estimates they are able to eradicate the virus in one in three individuals, thus halting carcinogenesis.

Lymphoma

Cells of the lymphatic system are uniquely susceptible to viral damage; several viruses, including simian virus 40 (SV40) DNA sequences, Epstein-Barr virus (EBV), and human herpesvirus-8 (HHV-8), have been linked to lymphomas.



Herpesviruses, including Epstein-Barr virus and human herpesvirus-8, may be particularly carcinogenic because they contain a multitude of genes that can prevent cell death. Shown here are various viruses from the Herpesviridae family, as seen through an electron microscope.

"Lymphocytes are supposed to take care of infection. By association, maybe they are also at risk for being affected by microbes," said Dr. Samaniego. "Nobody knows what comes first. Is it lymphoma that provides a place for the virus, or is it the other way around?"

The incidence of non-Hodgkin's lymphoma has increased over the past 30 years; 287,000 cases are diagnosed each year around the world. SV40, a monkey virus that contaminated early versions of the polio vaccine, was given to as many as 30 million people between 1955 and 1963. Evidence of SV40 DNA sequences has been found in non-Hodgkin's lymphoma and, infrequently, in other types of tumor cells.

"We don't know what the SV40 in the vaccine did to people. It could have vaccinated them against the virus, or it could have introduced it into people," said Dr. Samaniego. SV40 has also appeared in people who have never been vaccinated; it is spread from person to person through bodily secretions.

SV40, which like HPV works by inactivating p53 and Rb, is also associated with brain and bone tumors, mesotheliomas, and B-cell lymphomas. "We think it is an old virus in humans because whenever a new virus is introduced into a species, it usually causes severe illness. It kills people. SV40 doesn't harm people early on, but over time it may contribute to tumor development," Dr. Samaniego said.

Currently, Dr. Samaniego and others at M. D. Anderson are comparing the prognoses of SV40-positive and SV40-negative lymphomas. They are also checking tumors resected years ago for the presence of SV40 and testing lymphocytes in culture to see whether SV40 genes induce lymphoma.

Another virus associated with lymphoma is EBV, which causes mononucleosis in young adults. EBV is spread through saliva and may infect 80% of people worldwide. A recent study found that people who have contracted mononucleosis have double the risk of Hodgkin's disease. However, the risk is still low: only one in 1,000 young adults with mononucleosis will get Hodgkin's disease.

EBV infects the B cells of the immune system and produces a protein called LMP1 that mimics CD40, an important immune cell molecule. This allows the virus to manipulate immune cell regulation pathways for its own designs. EBV, which has been linked to invasive breast cancer, can also disable a cellular protein that normally suppresses malignant cell migration, thus allowing cancerous cells to metastasize.

Strangely, EBV infection is associated with distinct cancers in different regions of the world. In North America and Europe, EBV infection is linked to Hodgkin's disease, whereas in China it is linked to nasopharyngeal cancer and in Africa to Burkitt's lymphoma. Nearly all cases of Burkitt's lymphoma in Africa have evidence of EBV infection, compared with only 15% to 20% of cases in the United States. Environmental factors may play a large part in these unique manifestations.

EBV is one of many cancer-causing viruses that belong to the human herpesvirus family, the members of which also cause cold sores, genital herpes, and chicken pox. According to Dr. Samaniego, herpesviruses may be particularly carcinogenic because they contain a multitude of genes that can prevent apoptosis.

Another member of the herpesvirus family associated with lymphoma is HHV-8. Recently isolated, HHV-8 contains many human oncogene homologues, including cyclin D and bcl-2. One hundred percent of cases of primary effusion lymphoma and Kaposi's sarcoma contain HHV-8.

HIV and cancer: a symbiotic relationship

People infected with human immunodeficiency virus-1 (HIV-1) have an enormously increased risk of cancer, especially Kaposi's sarcoma and lymphoma. "With HIV infection, we have had a surge of new cancers," Dr. Samaniego said. "We have 40 million people worldwide infected by HIV, and

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about two million have some kind of cancer associated with HIV infection."

According to Dr. Samaniego, HIV-1 causes cancer indirectly and through more than one mechanism. One pathway to cancer involves the HIV-1 Tat protein, which allows HIV to replicate itself many times over. HIV-1 Tat is known to activate several genes that make cells prone to cancer. In one study at M. D. Anderson, Dr. Samaniego introduced Kaposi's sarcoma cells into transgenic mice expressing HIV-1 Tat. The mice with Tat expressed higher levels of inflammatory and growth-promoting cytokines and grew bigger tumors than did the control mice.

Additionally, HIV-1 appears to travel with and enable other oncogenic viruses such as HHV-8. Dr. Samaniego and others at M. D. Anderson have conducted several studies of the relationship among HHV-8, HIV-1, and Kaposi's sarcoma. They found that K1, a gene in HHV-8, interacts with HIV-1 Tat to promote inflammation, which may play an important role in advancing Kaposi's sarcoma. "What you find is that HIV-1 infection allows other viral infections to spread, and most of these viruses are associated with cancer," said Dr. Samaniego.

Viruses and Associated Human Cancers

Virus	Type of Cancer		Cofactors
Epstein-Barr virus (EBV)	Burkitt's lymphoma	→	Malaria
	Nasopharyngeal carcinoma	→	Nitrosamines
	B-cell lymphoma	→	Immunodeficiency, HIV-1
	Hodgkin's disease	→	Unknown
	Breast cancer (suspected)	→	Unknown
Hepatitis B virus (HBV)	Liver cancer	→	Aflatoxin, alcohol
Hepatitis C virus (HCV)	Splenic lymphoma	→	Unknown
	Liver cancer	→	Aflatoxin, alcohol
Human herpesvirus-8 (HHV-8)	Kaposi's sarcoma	→	HIV-1
	Primary effusion lymphoma	→	EBV and HIV-1
	Multicentric Castleman disease	→	HIV-1
Human papillomavirus (HPV)	Cervical, vulvar, vaginal, penile, anal, skin, oropharyngeal	→	Smoking, oral contraceptives, multiparity, other sexually transmitted diseases
Human T-cell lymphotropic virus type 1 (HTLV-1)	Adult T-cell leukemia/ lymphoma (ATL)	→	Unknown
Simian virus 40 (SV40)	Mesothelioma	→	Asbestos
	Non-Hodgkin's lymphoma, brain and bone tumors, and B-cell lymphomas (suspected)	→	Unknown

Gastrointestinal cancers

After years of dispute, scientists now agree that *Helicobacter pylori*—a bacterium, rather than a virus, that causes 90% of duodenal ulcers—also causes 40% to 60% of all gastric cancers. This finding has prompted researchers to take a closer look at other infectious agents that may contribute to cancers of the gastrointestinal tract.

Two likely suspects are the human cytomegalovirus and the JC virus. The human cytomegalovirus, a typically asymptomatic herpesvirus that is transmitted through bodily fluids and infects 40% of the population in the United States, has been found in 85% of colon cancer cells. It has also been found in brain tumors. The JC virus, a polyomavirus found in 80% of adults, has been found in 89% of colon cancers. Also asymptomatic, the JC virus is believed to infect people through the oral-fecal route.

Viral treatments

The good news about the role that viruses play in carcinogenesis is that vaccines now hold great promise in preventing and treating cancer. Indeed, vaccines against HPV and HBV may decrease the global cancer incidence by 15%; the vaccine for HBV has already had a major impact on the rates of hepatocellular carcinoma. Researchers also are working to develop vaccines for HIV-1 and EBV, as well as for HCV.

Furthermore, viruses may also be used to deliver gene therapy to patients with cancer and other illnesses. At M. D. Anderson, Dr. Bresalier and his colleagues are studying the use of viruses as vectors to deliver tumor necrosis factor directly to esophageal adenocarcinomas. "The idea is that this will spread the agent within the tumor and cause either necrosis of the tumor or sensitize the tumor to radiation treatment," said Dr. Bresalier.

"I think the wave of the future is how viruses can be supportive in therapy," said Dr. Samaniego. "We are looking for effective ways of preventing lymphoma and other cancers, so I think a lot of what you will see in the next few years is going to be [using viruses as therapy]. It is going to be a low-cost modality that is applicable worldwide." ●

For more information, *contact Dr. Samaniego at (713) 792-2860, Dr. Tortolero-Luna at (713) 745-2352, or Dr. Bresalier at (713) 745-4340.*

HOUSE•CALL

Cancer and Your Weight

Lately, it seems that almost every week, a new study comes along that links obesity to another health problem. Now, an American Cancer Society (ACS) study has found that excess pounds can increase a person's risk of dying from cancer. But don't despair, you can take steps to counteract this risk and improve your overall health.

In the ACS study, 900,000 people were evaluated for 16 years. The study participants who were overweight or obese were compared with those who were of normal weight, with adjustments made for smoking and other cancer risk factors. A body mass index (BMI) of 18.5 to 24.9 was considered normal, a BMI of 25 to 29.9 was overweight, and a BMI of 30 or above was obese. By this measure, a 5-foot-11-inch person who weighs 175 pounds would be in the normal range, with a BMI of 24.4. A 5-foot-5-inch woman weighing between 150 and 174 pounds and a 6-foot man weighing between 182 and 213 pounds would both be in the overweight range, and people with weights above that would be classified as obese.

None of the participants had cancer at the beginning of the study, but by the end of it, a substantial number did.

The researchers concluded that excess weight could account for 14% of cancer deaths in the men studied and 20% in the women. The ACS study linked excess weight to the occurrence of non-Hodgkin's lymphoma, multiple myeloma, and cancers of the cervix, ovary, liver, pancreas, stomach, and prostate. Earlier studies have found that being overweight is associated with cancers of the breast and uterus, colon and rectum, kidney, gallbladder, and esophagus.

No matter how much you weigh, however, the following actions will help to decrease your chances of getting cancer:

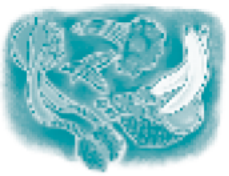
■ Maintain your weight within the normal body mass index range.

If you are already overweight, consult your physician for a safe weight-loss plan. Even losing as little as 5% to 10% of body weight has been shown to decrease the risk for many diseases.

■ Exercise frequently—preferably every day.

Studies have revealed that regular exercise dramatically reduces the risk of colon and breast cancer and may lower the risk of cancers of the prostate, endometrium, kidney, and lung.

How much exercise do you need? The American Institute for Cancer Research's report "Food, Nutrition, and the Prevention of Cancer" recommends one hour of moderate activity a day plus one additional hour per week of vigorous activity such as brisk walking uphill, swimming, playing tennis, or dancing. While this may sound a bit overwhelming, keep in mind that moderate exercise includes such everyday activities as doing housework, playing with your kids, raking leaves or gardening, taking the stairs instead of the elevator, and taking an after-dinner walk.



■ Eat lots of fruits and vegetables.

The antioxidants, carotenoids, and vitamins C, A, and E found in fruits and vegetables have been shown to reduce the risk of a variety of cancers. The National Cancer Institute advises eating five or more servings of fruits and vegetables a day. One serving is one medium piece or 1/2 cup of fruit, 3/4 cup of 100% fruit or vegetable juice, 1/4 cup of dried fruit, 1/2 cup of raw or cooked vegetables, or 1 cup of leafy vegetables.

■ Increase your consumption of low-fat, calcium-rich foods.

Recent studies indicate that calcium may help prevent colon cancer. A National Institutes of Health consensus panel of experts recommended that adult men and women have a calcium intake of 1,000 mg daily. After age 51 for women and 65 for men, the daily calcium intake should increase to 1,500 mg. One cup of milk contains 300 mg of calcium, and 1 cup of nonfat plain yogurt contains 400 mg.

These simple changes in diet and exercise can go a long way in protecting you against cancer. ●

For more information, contact your physician or contact the M. D. Anderson Information Line:

(800) 392-1611, Option 3, *within the United States, or*

(713) 792-3245 *in Houston and outside the United States.*

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Treating Breast Cancer during Pregnancy

Karin M.E.H. Gwyn, M.D., Assistant Professor
Richard L. Theriault, D.O., Professor
Department of Breast Medical Oncology

Since 1989, more than 50 pregnant women with breast cancer—the largest known prospective cohort—have been enrolled in a treatment protocol at M. D. Anderson Cancer Center. What follows is a summary of what we have learned.

A review of our experience found mammography (with abdominal shielding) and breast ultrasonography in pregnant women to be quite effective at diagnosing abnormalities and assessing the extent of local disease. A core biopsy of the lesion is the method we most commonly use to diagnose invasive breast cancer. These biopsies should be interpreted by a pathologist familiar with the changes that occur in the breast during pregnancy.

Patients with clinically advanced breast cancer should be evaluated for metastatic disease. Our approach is a chest X-ray (with abdominal shielding), ultrasonography of the liver, and magnetic resonance imaging, without contrast, of the spine after the first trimester. Because of concerns about radiation exposure, we try to avoid using computed tomography and bone scans.

Treating a pregnant woman with breast cancer requires a team of professionals that includes specialists in maternal and fetal health. Ultrasonography is used to determine fetal age and development and the expected date of delivery because they have a significant impact on treatment planning.

Breast surgery can usually be performed with minimal risk to the fetus. The radiation therapy required to complete breast conservation surgery is contraindicated during pregnancy, although breast conservation is possible in women who are diagnosed in the third trimester or whose cancer warrants preoperative chemotherapy.

The indications for systemic therapy are the same as those in a nonpregnant patient. We believe that combination chemotherapy with 5-fluorouracil, doxorubicin, and cyclophosphamide is generally safe in the second and third trimesters. We avoid chemotherapy during the first trimester because the risk of fetal exposure is too high. We also avoid the use of methotrexate, an abortifactant, and we do not use taxanes or tamoxifen because their safety in pregnant patients has not been established.

The limited data available do not support the belief that pregnancy termination improves the survival of patients with breast cancer. However, in cases of known or suspected fetal teratogenesis or if maternal health is in jeopardy, it may be appropriate.

We continue to evaluate and treat pregnant women with breast cancer as part of our ongoing clinical protocol and to follow up on both our patients and their children to determine the effectiveness of therapy as well as the long-term effects of in utero chemotherapy exposure.

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