bronchoscopy program at the British Columbia Cancer Agency of Vancouver. The other participating centers are in France, Germany, and the Netherlands.

In Lam’s approach, patients are first screened using sputum cytology (see News, Dec. 17, 1997). If abnormal cells are detected, the patient then has a fluorescent bronchoscopy and a biopsy to pinpoint the tumor’s location and confirm that it has not already become widely invasive.

**Measuring Fluorescence**

A new bronchoscope invented by Lam and colleagues uses blue light, which induces tissue to fluoresce weakly, Lam explained. Cancerous tissue fluoresces slightly less than normal tissue, a difference the Vancouver scientists exploited by designing a special camera — approved by FDA in 1996 — that picks up this subtle contrast to localize the lesion. The device is called Life-Lung and is made by Xillix Technologies of Richmond, B.C.

Roswell Park is planning a trial of early detection using sputum cytology and the fluorescent bronchoscope in patients previously treated for lung or head and neck cancer. Patients discovered to have new lung cancers will be treated with PDT or other modalities depending on what is most appropriate for each.

“I predict that in coming years more microinvasive cancer will be found and will be treatable with photodynamic therapy,” Lam said.

Meanwhile, researchers at the Mayo Clinic in Rochester, Minn., and Jacksonville, Fla., are testing PDT for another group of early stage lung cancer patients, who have squamous-cell lung cancers that have not penetrated the bronchial wall. Surgery is the usual treatment for these patients, but it carries the risk of complications such as loss of pulmonary function when substantial sections of lung are removed.

“Our hypothesis was that photodynamic therapy could reduce the risk of surgery, preserve lung tissue, and decrease costs without sacrificing therapeutic effectiveness,” said Denis A. Cortese, M.D., of Mayo Jacksonville. “Our goal was to evaluate the effectiveness of photodynamic therapy by determining how many patients could ultimately be spared surgery.”

In an article published in the July 1997 Mayo Clinic Proceedings, Cortese and colleagues reported that nine of 21 patients were treated successfully with PDT and spared surgery, with 2 to 10 years of follow-up.

A similar trial on PDT as an alternative to surgery is being conducted in Japan, and interim analysis “lends further support to the concept that PDT is an effective alternative to surgical resection,” Harubumi Kato, M.D., Ph.D., of Tokyo Medical College wrote in an editorial on the Cortese study.

In an earlier study, Kato and his colleagues found that PDT is more cost-effective than surgery for early stage lung cancer. The total cost per surgically treated patient was $14,948, while the cost per patient treated with PDT was $8,475.

— **Tom Reynolds**

**Infections and Cancer: Viruses Are Still Prime Suspects**

If a mouse can get breast cancer from a tumor virus, can this happen in humans, too?

This is an old question, but at the 8th International Congress on Anti-Cancer Treatment in Paris, James Holland, M.D., distinguished professor of neoplastic diseases at Mount Sinai Medical Center in New York, thinks he is closer to the answer with his discovery of a “cousin” to the mouse mammary tumor virus in human breast cancers. Sequences of the virus, which he calls the Human Mammary Tumor Virus (HMTV), were found in more than a third (37%) of a series of 387 fresh or frozen breast cancer tissues.

When it comes to breast cancer, the finger of suspicion is also cast on the Epstein-Barr virus, according to studies reported by Beverly Griffin, Ph.D., D.Sc., of the Department of Infectious Diseases at the Imperial College School of Medicine at Hammersmith Hospital in London. Examination of several hundred breast cancers from patients in Europe and Africa found EBV in anywhere from 20% to 46% of the specimens in geographic subgroups.

Whether or not additional investigations confirm that HMTV, EBV, or any other virus is indeed implicated as a
cause of breast cancer — perhaps with a boost from a few cofactors — the whole idea of infections causing cancers of various types has once again resurfaced, as demonstrated by a special symposium at the Paris meeting as well as by reports piling up in the literature. Moreover, additional research dollars are being spent to more closely examine the whole question of infections and cancer.

“We’re increasing our investment in this,” National Cancer Institute director Richard Klausner, M.D., said. “In fact we’re developing a new section at NCI on infectious causes of cancer.”

As for Holland’s report, Klausner called it, “intriguing,” but in need of confirmation from other laboratories.

A Lengthy Search

“The search for a breast cancer tumor virus in humans has been a goal for 30 or 40 years,” commented Gabriel Hortobagyi, M.D., professor and chairman of the Department of Breast and Gynecologic Medical Oncology at the University of Texas M. D. Anderson Cancer Center, Houston. Hortobagyi was co-director of the meeting, which was also sponsored by the medical oncology service of the Pitié Salpêtrière. Hortobagyi said Holland’s work was, “very exciting” and “we need to follow up on that.”

Robert Gallo, M.D., of the Institute of Human Virology at the University of Maryland, Baltimore, also commented that the Holland study needs to be verified. He said that Holland, “didn’t show [that the virus] was transmitted by milk, but if it’s like the mouse, it is.”

He added that breastfeeding transmission is implicated in another virally induced cancer — that caused by human T-cell leukemia virus (HTLV-I) that is endemic to areas such as southern Japan. He said he would personally advise that a woman carrying that virus not breast-feed. “The Japanese have reduced the incidence of HTLV-I transmission by stopping breast feeding,” Gallo said.

This whole question of whether viruses or other agents can cause cancer has investigators concerned, several suggested, because of fears that the public will misinterpret what is meant by “infectious.” Klausner was quick to state boldly that “cancer is not contagious.”

What is contagious, however, are the many infections that already have been shown to lead in many cases to cancer.

For instance, Harald zur Hausen, M.D., of the German Cancer Research Center in Heidelberg, a world expert on papillomaviruses, emphasized that people should know that the premalignant...

Stat Bite


The American Cancer Society, the National Cancer Institute, and the Centers for Disease Control and Prevention have produced a “Report Card” to the nation on progress related to cancer prevention and control in the United States. This report, which appears in the March 15 issue of the journal Cancer, shows that incidence rates for the four major cancer sites and for all sites combined rose from 1973 to 1990 but are now declining for all sites and for prostate, lung, and colorectal cancer.

Annual percent change, all ages, all races

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<tr>
<td>All sites</td>
<td>+1.2</td>
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*Annual percent change is based on gender-specific rates.
Note: Incidence rates are age-adjusted to the 1970 U.S. standard population.
nant lesions of the cervix are infectious. This is not the case for malignant lesions, so the cancer itself is almost uniformly noninfectious.”

He also said that more than 150 different genotypes of the papilloma virus are likely to exist, with 82 already sequenced and another 70 viruses partially characterized. Not all of these have oncogenic potential, he added, and even those individuals who are infected with high-risk viruses like HPV 16 will not necessarily develop a tumor. “In many of these cases the virus clears because of immune intervention, or in some cases even the persistence of the virus does not lead to a malignant tumor,” he said. “We calculate from our German data that of 100 infected patients over a period of 45 years, only 6% eventually developed cervical cancer.”

Vaccines under development, zur Hausen said, have the potential to prevent malignant transformation in perhaps 15% of women at risk of cervical cancer. He added that there do not seem to be cofactors involved in progression to malignancy, but rather that, over time, the viruses mutate at varying rates. So far, papillomaviruses have been implicated in malignancies of the upper GI tract as well as the lower genital tract.

As for the role of the Epstein-Barr virus, Griffin said that cofactors do appear to be involved, such as the link between nasopharyngeal cancer in China and a salty fish diet, or perhaps a genetic predisposition. “EBV is not itself fully oncogenic,” she said. “You need cofactors in every case, and I think we need to spend more time to find these.”

At the same time, “we conclude that the EBV has more oncogenic potential than we realized. Most studies have been in the B-cell environment, but we ought to look at it also in carcinomas. We need to return to the epithelial cell environment.”

**EBV’s Role**

She said that so far EBV correlates 100% with poorly differentiated nasopharyngeal carcinoma, Burkitt’s lymphoma and salivary gland lymphoepithelioma. There are also correlations with Hodgkin’s disease of from 50% to 60%, with American Burkitt’s lymphoma of about 20%, and with breast cancer from 20% to 45%, “if ultimately confirmed.” For highly differentiated nasopharyngeal carcinoma, she added, the correlation is only about 20%, “making us think that the state of differentiation of the cell, and the type of cell, has an effect on viral gene expression and what the virus will do in this particular cell.”

Griffin also put forth the proposition that EBV may not necessarily be seen in the tumors themselves because it has caused oncogenesis by “hit and run.” She said it can be shown in vitro that EBV can immortalize a cell and then go into hiding.

Altogether, investigators reported a fairly extensive list of cancer-related infections, including the lymphomas and the Kaposi’s sarcomas and other cancers associated with HIV infection, stomach cancer from *Helicobacter pylori*, and those cancers that can result from hepatitis infection, and which are in some cases vaccine preventable.

— Jean McCann

### Lessons From the Tobacco Wars Edify Nutrition War Tactics

Advocates of improved diet and exercise for better cancer prevention are calling for policy changes and physician training to help the public make the kind of lasting improvements that might reduce cancer rates. They hope to bypass the excruciatingly arduous and long path that anti-tobacco advocates had to travel before warnings about the hazards of smoking took hold.

Although the evidence was clear that cigarette smoking caused lung cancer as early as the 1950s, physicians were slow to take up the cause, according to Ernst L. Wynder, M.D., an investigator in the initial tobacco and lung cancer studies. Thirty years passed before political activists began to support legislation to curb tobacco use.

Evidence for the impact of diet and exercise on cancer risk has been building over the years. Although research is still equivocal about the effect of specific nutrients and types of fat, broad recommendations, such as eating more fruits and vegetables and maintaining a healthy weight, are widely supported.

But consensus of opinion among medical experts is not enough to create action unless it is translated into prevention and control measures by government, the media, physicians, and educators, according to Wynder, founder and...