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CHICAGO TRIBUNE

Mystery of the monkey virus
Loyola pathologist probes link to cancer, polio vaccine; feds say it's harmless
By Peter Gorner
Tribune science reporter

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As controversy swirls about him, Loyola University pathologist Michele Carbone stays focused on his research, unraveling the secrets of a rogue monkey virus.

Simian virus 40, or SV−40, is a medical mystery looming at the borders of science's ability to determine the causes of cancer. It is at the center of a controversy now because so many people are potentially infected by the virus, which crossed over from monkeys to humans as a then−unknown contaminant of the polio vaccine.

The virus, the government said, is harmless. But it keeps showing up in human cancers, and some researchers say it may contribute to as many as

60,000 U.S. deaths a year.

Only a handful of viruses had been associated with human cancers, and none of them were simian in origin. But whether SV−40 is causing tumors or just is an innocent by−stander collected by them remains the critical, and heretofore unanswered, question.

To Carbone, the answer seems clear.

"The perfect little war machine," Carbone said of SV−40. "The most oncogenic [cancer−causing] virus we know of. I definitely wouldn't want it in my body."

SV−40 jumped the species barrier more than 40 years ago when it contaminated batches of Salk polio vaccine, which were grown on monkey kidney cells.

The virtual eradication of polio as a major childhood killer and crippler was one of the triumphs of public health. But today, as many as 12 million Baby Boomers who received polio inoculations may have SV−40 in their bodies, according to estimates.

Federal health officials insist there's no problem. Studies conducted since SV−40 was discovered in 1960 have found no increase in cancer among those who were vaccinated against polio as children.

"Over 98 million Americans received one or more doses of polio vaccine during the period (1955−1963) when some of the vaccine was contaminated with SV−40," the Centers for Disease Control and Prevention said in a statement. "SV−40 has been found in certain types of human cancers, but it has not been determined that SV−40 causes these cancers. The majority of evidence suggests there is no causal relationship between receipt of SV−40−contaminated vaccine and cancer; however, some research results are conflicting and more studies are needed."

But Carbone has spearheaded a growing scientific consensus. His research −− supported by more than 70 confirmatory studies from 60 different laboratories worldwide −− indicates that SV−40 could be a factor that predisposes some people to develop tumors of the brain, bones, lymph glands and tissue that surrounds the lungs.

Interest in Carbone's work is being fueled by a new book, "The Virus and the Vaccine," by journalists Debbie Bookchin and Jim Schumacher. Carbone is credited with the revitalization of interest in SV−40, and to him, the most important association is with mesothelioma, a particularly deadly form of lung cancer.

Carbone, 44, has been investigating SV−40 since the early 1990s when he was a young researcher at the National Cancer Institute testing how viruses could cause cancer in laboratory animals. He injected hamsters with SV−40. They kept developing cancer, dying within a few months from rare tumors called mesotheliomas that affect the cells lining the chest and lung.

"Mesotheliomas? Why would this virus cause this rare cancer and not cause cancers in all the other tissues that had been exposed to the virus through the bloodstream?" Carbone said. "I kept repeating the experiment. Same thing."

Here was a medical mystery worth investigating. For Carbone, the urge probably was inborn.

The son of a prominent orthopedic surgeon in Italy and the latest in a line of seven generations of physicians, Carbone grew up in the southern province of Calabria. He spent many hours in the family library poring over mysterious and lavishly illustrated medical texts −− some of them 300 years old −− that had been accumulated by his ancestors.

After graduating at the top of his class in 1984 from the University of Rome Medical School, Carbone was awarded a coveted National Institute of Health doctoral fellowship and began the painful trek for recognition as a research scientist.

His rise has been rapid −− honors include a knighthood from the Italian government −− but SV−40 research seems to provoke unusual hostility that probably would have crushed a less confident individual.

The main cancer associated with the virus, malignant mesothelioma, is found primarily in older men who have spent most of their working lives in plants manufacturing asbestos products. The disease was practically unknown until 1950. It kills about 3,000 Americans a year.

A paper published by Carbone and his colleagues in 1994 was the first to systematically isolate SV−40 in human mesotheliomas. The scientists proposed the virus might work in partnership with asbestos in susceptible individuals, somehow helping the mineral fiber cause cancer.

Carbone also noted that as many as half of the Americans diagnosed with mesothelioma each year have no history of asbestos exposure and suggested that perhaps SV−40 could cause cancer on its own.

And, Carbone felt compelled to point out, the increase in mesotheliomas over the last 30 years not only paralleled the expanding use of asbestos but also coincided with the inadvertent contamination of polio vaccine.

Such findings received a chilly reception from his superiors at NIH.

"I got the impression that this was something that people did not like to hear −− the polio vaccine could cause this cancer," Carbone said.

He emphasizes that most people who carry SV−40 in their cells won't develop cancer because a healthy immune system would destroy the virus.

"But if we knew this virus was responsible for cancer, that would mean we had a new treatment target for mesothelioma research −− a glimmer of hope.

To me, that's the important point," said Carbone.

In a series of papers published from 1992 through 1996, Carbone showed that SV−40 inhibited the protective tumor suppressor genes called p53 and rB in human mesotheliomas.

Normally, the job of those genes is to prevent a cell from dividing uncontrollably, or to destroy it when it gets too damaged by mutations and could become cancerous.

Transforms cells

"But mesothelial cells are different from other cells. They have unusually high levels of p53. We found the virus replicates very slowly in them and doesn't kill the cells, but it transforms them," Carbone said.

The virus sets up the cell to become malignant, but then something else must happen to trigger cancer −− some co−carcinogen must occur.

In 1999, Carbone identified SV−40 genes and proteins in as many as 83 percent of human patients with mesothelioma. He pieced together the viral and cellular mechanisms that make such cells uniquely vulnerable to SV−40.

The study marked the first time that researchers had presented direct evidence that linked a long−forgotten source of polio vaccine contamination and a cancer that primarily affects people several decades later.

"We found that the monkey virus and asbestos fibers are co−carcinogens −− which seemed crazy when we discovered it," Carbone said. "What could be more different than an asbestos fiber and a monkey virus?

"Yet together they cause one of the deadliest of all human cancers." In other studies, Carbone and fellow researchers suggested SV−40 raises the risk of several rare cancers −− as well as for non−Hodgkin's lymphoma, the fifth most common malignancy in the U.S.

This cancer of the lymph system has confounded physicians by doubling in incidence over the last 30 years.

"There's no disagreement about the fact that this virus was massively transferred into humans from 1954 to 1963," Carbone said. "More often than not, viruses become more dangerous when they transfer species."

Animal viruses are trouble

"We've had millions of years to adapt and live in symbiosis with our own viruses. But as we have seen with HIV, Ebola, SARS, etc., animal viruses can cause big trouble."

Home base for Carbone is Loyola University's Medical School and Cardinal Bernardin Cancer Center in Maywood, where his days are spent pursuing the

quest −− in addition to performing autopsies, holding seminars and running off to teach karate classes (Carbone earned black belts in three martial arts).

Evenings are spent with his wife and young daughter in the family's 1893 Frank Lloyd Wright house in Oak Park.Carbone realized early on that SV−40's relationship with cancer is probably not going to be cause and effect.

"I think it's a factor that contributes to the final event," he said.

"For instance, 94.6 percent of the people who work with asbestos all their lives don't get cancer. But what about those who do? Did they just have bad luck or were other factors contributing?"

SV−40 could be one factor. The other factor was discovered by Carbone and his team in three remote villages in Turkey where mesotheliomas are known to cause more than 50 percent of cancer deaths. Surrounding villages seem to be unaffected.

"What we found was that the disease was genetically transmitted. In certain households, everybody died of it. Next door, nobody did."

The researchers looked for SV−40, but couldn't find it. They looked for asbestos, but discovered it was a natural component of the volcanic soil and was found virtually everywhere. What could account for the uniquely high numbers of mesothelioma in the two villages?

"We implicated a building material called erionite, a mineral fiber like asbestos that was found in the lungs of several villagers.

"However, erionite also was common in the area and couldn't by itself account for the high incidence of mesotheliomas," Carbone said.

The scientists concentrated on the homes where entire families had died of the disease. "The houses of death," residents called them.

To gather genetic information about the haunted families, the team gradually pieced together a family pedigree of 526 people, consisting of 22 affected nuclear families with 87 children, 41 of whom had developed mesothelioma as adults.

In these families, mesothelioma is passed along via a dominant gene, Carbone discovered: One either inherits the deadly susceptibility or one escapes. Building materials may be a co−factor in genetically predisposed individuals.

"The power of this gene is so strong that we have a good chance to isolate it. I don't think the gene will be a curiosity limited to those unfortunate families in Turkey.

"Here, it's probably mutated because of the action of other carcinogens such as asbestos, radiation and SV−40."

However, prominent cancer researcher Dr. Nicholas J. Vogelzang, director of the Nevada Cancer Institute, said the evidence, though suggestive, does not prove SV−40 is causing trouble.

"Nobody knows why SV−40 genetic material is being detected in the cancers, but there have been no excess cancer rates," Vogelzang said.

"Does that mean it doesn't play a role? No. As scientists say, the absence of proof is not the proof of absence.

"But the steps from laboratory observations to public health policies are long and difficult. Ultimately, it comes down to very hard−core labor, slogging through medical records and doing the epidemiology."

But then Vogelzang paused.

"The only thing that worries me a bit is the increase in lymphomas."

Two years ago, Texas researchers linked SV−40 to non−Hodgkin's lymphoma. Baylor University's Dr. Janet Butel, leader of the team, has changed her attitude about the monkey virus. She became a convert.

"I believe that SV−40 is causing infections in humans today," said Butel, head of the department of molecular virology and microbiology at Baylor.

She said she will not let 40 years of federal orthodoxy deter her. It takes a long time to change a paradigm, she said.

"But we know the role of HIV in Kaposi sarcoma. We know about human papilloma virus and cervical cancer. We know about hepatitis B and hepatitis C in liver cancer.

"I think SV−40 belongs on the list."

Right now, Carbone said his research is most relevant to SV−40 and mesothelioma, although broader implications for cancer are his aim.

"It looks very complicated −− SV−40, asbestos, your genetic predisposition," Carbone says. "But by uncovering these variables, we're creating new options for prevention and therapeutic approaches.

`Change one variable'

"We only have to change one variable −− screen for the gene, vaccinate against the virus, get rid of asbestos −− to dramatically affect the risk of cancer."

"Otherwise, we're paralyzed. We know that asbestos, for example, is going to cause cancer in 5 percent of us. Without having a clue about why that happens, we will be living in fear, watching each other's eyes.

"Who will get cancer? Will you? Will I?"

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How the monkey virus could generate cancer cells

Recent research suggests that a person's exposure to a combination of simian virus 40 (SV−40) and asbestos could increase the risk of cancer. The body's immune system usually can detect SV−40 and kill the infected cell. But because asbestos impairs immune response, the infected cell is more likely to escape detection.

1. Simian virus (SV−40) enters a healthy cell. Simian virus, Chromosome, Healthy cell, Nucleus.

2. The virus begins to make its own proteins, which interfere with the healthy cell's proteins that balance growth. DETAIL −− Infected cell. Some viral proteins activate the cell's proteins that stimulate growth. Other viral proteins deactivate the proteins that prevent abnormal growth.

3. If asbestos is present, it activates another set of special proteins that stimulate rapid division of the malignant cell.

4. The resulting malignant cell continues producing more damaged cells and can develop into a tumor. Malignant cells.

Source: Dr. Michele Carbone, Loyola University Medical Center

Haeyoun Park and Phil Geib/Chicago Tribune

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Questions about contamination

Blood tests can identify antibodies to SV−40, but at this time there is no way to tell if someone is infected by the virus and no recommended treatment, Michele Carbone said.

People who are concerned about polio vaccine contamination by SV−40 and their health may call the Food and Drug Administration at 800−835−4709. Carbone is willing to receive questions at his office via fax: 708−327−3238; or via e−mail: therma1@lumc.edu.