

Virus-Cancer Crosspoint

New evidence points to virus antibodies as cancer-causing catalysts in certain predisposed humans

BY JOAN AREHART-TREICHEL

Although viruses have been shown to trigger a number of animal cancers, their link with human cancers has been less certain. Now a massive four-year population study in Africa, conducted by scientists from three continents, provides some of the strongest evidence yet that one kind of human cancer at least is caused by a virus. The study is unprecedented in that it involved the screening of people's blood for a virus before they were afflicted with cancer, thus opening the possibility of indicting the virus as a cancer-causing agent and suggesting ways of preventing infection with it.

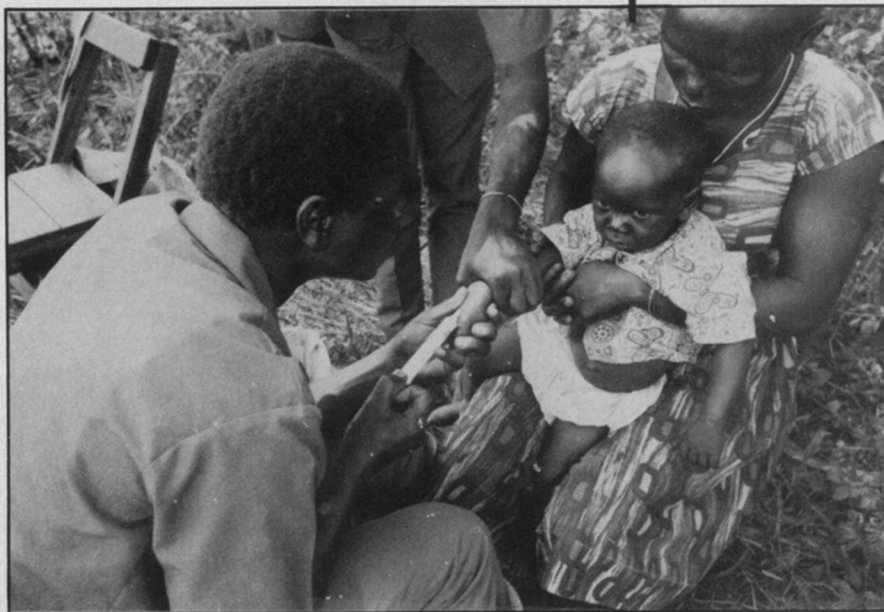
The results of the study were presented at the 7th International Symposium on Comparative Leukemia Research held recently in Copenhagen (SN: 10/25/75, p. 260), by Dr. Guy de Thé of the International Agency for Research in Lyon.

So far, the strongest link between a virus and human cancer has been between the so-called EB (Epstein-Barr) virus and several cancers of lymphoid organs—Burkitt's lymphoma and nasopharyngeal carcinoma. While the EB virus cannot be detected in human tissues, antibodies to the virus can.

Finding virus antibodies in people after they come down with these two kinds of cancer, however, is not sufficient proof that those viruses cause the cancers. Better proof would consist of detecting virus antibodies in people without the cancers, then watching to see whether those with especially high levels of antibodies come down with the cancers. Consequently that is what de Thé and his fellow team members in Europe, Africa and the United States attempted to do.

The study, which was done in Uganda, involved 70 scientists from Uganda, Europe and the United States. Some of the principal investigators, besides de Thé, included: Peter Tukei of the Ugandan Virus Institute, Charles Olweny of the Ugandan Cancer Institute, Werner Henle of Children's Hospital in Philadelphia, Richard Morrow of the Harvard School of Public Health in Boston and George Klein of the Karolinska Institute in Stockholm.

The study was conducted under the auspices of the World Health Organization. It cost \$1.5 million, 90 percent of



One of thousands of Ugandan children that were treated for Burkitt's lymphoma.



One case, before and after treatment.

which was paid by the U.S. National Cancer Institute.

In 1971, they arranged to study 40,000 children aged two to five years old in Uganda—specifically, to see whether children with the virus eventually came down with Burkitt's lymphoma. Uganda was selected for the study because Burkitt's lymphoma is endemic in that region of the world. The reason that so many children were needed to get meaningful results is that Burkitt's lymphoma, although endemic, is still relatively uncommon in Uganda.

Such a large population study to link human cancer with a virus has never been conducted before, because it is terribly costly, takes several years at least to complete and requires the cooperation of a number of scientists from various specialties. And in the case of studying hundreds of thousands of children in Uganda, it also involved actually getting out in the bush to draw blood samples and to see whether the children eventually got Burkitt's lymphoma. "We had to be willing to give blood and sweat, or we never

would have been successful," de Thé admits. "It was a fantastic challenge."

In 1972, de Thé and his team started drawing blood samples from the children. By September 1974 they had finished. All of the children were found to have EB virus in their bloodstreams, suggesting that the virus is rampant in Uganda. Then the investigators looked for Burkitt's lymphoma in the children. Eight of the children were found to have come down with Burkitt's lymphoma since the study started. All of them had had, prior to getting cancer, levels of EB virus antibodies in their blood that were twice as high as the levels in the other children. "So it is very clear," de Thé says, "that these children are reacting differently to the virus."

Infectious mononucleosis also appears to be caused by the EB virus. However, no antibodies against EB virus are found in "mono" patients. In other words, EB virus is apparently able to cause cancer when it strikes people early in life. Why only some Ugandan children are susceptible, however, remains to be determined.

So how can Ugandans be protected from Burkitt's lymphoma? There are several possibilities. One is better hygiene for young children in Uganda. Such hygiene, de Thé believes, could wipe out Burkitt's lymphoma in that country. Another possibility is to see whether there is some other factor that predisposes Ugandans to EB virus infections and Burkitt's lymphoma. The reason that such a factor may exist is that EB infections are common throughout the world, but only Ugandans get Burkitt's. The third possibility, which would probably be best, would be to vac-

World Health Organization

ciate Ugandan children against the EB virus.

Developing an EB virus vaccine, though, is not yet possible. The virus cannot yet be grown in large amounts in tissue culture. And even if it could, and a vaccine could be made from the virus, there would be the ethical problem of giving a live cancer vaccine to people. Such a vaccine might cause cancer in people rather than prime their immune systems against cancer.

The ideal thing, de Thé explains, would be to extract proteins from the surface of

the EB virus and to use the proteins as a vaccine. That way the genetic core of the virus would not be used and would not have the opportunity of causing cancer. The viral proteins alone could serve as antigens to prime a person's immune system against EB virus and EB virus-caused cancer. De Thé and his colleagues are now attempting to purify such viral proteins so that they can be used as a vaccine.

Such a vaccine, de Thé says, would also help protect Americans and Europeans who have had mono against Hodg-

kin's disease. One of the members of his team has found, from a study in Scandinavia, that people who have had mono have five to six times the chance of coming down with Hodgkin's disease than do other people. Hodgkin's disease is related to Burkitt's lymphoma and nasopharyngeal carcinoma. It is cancer of the lymph nodes. An EB virus vaccine, de Thé says, would also be a boon to people in Southeast Asia who are susceptible to nasopharyngeal carcinoma. In fact, nasopharyngeal carcinoma is the most common cancer in Southeast Asia. □

OFF THE BEAT

With Scientists on the Østergade

Gray skies, chill winds, trees around Hamlet's castle in Elsinore turning yellow. It's October in Denmark. Copenhagen is different this October, however. The city has been inundated by some 300 scientists from throughout the world for the 7th International Symposium on Comparative Leukemia Research, sponsored by the Leukemia Society of America and the U.S. National Cancer Institute.

The scientists at this meeting are something to behold. Having relinquished their ivory towers, centrifuges, chromatographs and electron microscopes, they are catapulted into the real world of science politics, confrontation with peers of various scientific persuasions, the arts and even swinging night life. In brief, their human qualities, which are often masked by cerebral overexertion and scientific reticence, have become refreshingly apparent. For instance, they can be heard exchanging tips on how to get research money whether they're from Kalamazoo or Paris. The scientists can be seen downing Carlsberg and Tuborg beer, attacking lavish smorgasbords with vigor, arguing whether monkeys can give cancer to people and vice-versa. They can be seen taking in the Danish modern ballet "*Dødens Triumf*" (Triumph of Death), complete with nudes and acrid smoke from hell billowing from the stage. The attending experts can even be spied slipping into pornography shops along the Østergade and other streets that comprise Copenhagen's mall.

Small, humorous incidents reveal their humanness still further. It's the opening of the first session of the symposium, and Dr. N., who is in charge at this point, announces: "Ladies and gentlemen, since this is a cancer meeting, I suggest that we refrain from smoking during it." Chain smokers throughout the room look chagrined and reluctantly put out their Kents, Gauloises or whatever. A pipe smoker hastily shoves his lit pipe into his

pocket. The scientist seated next to him expects him to go up in smoke any minute.

Break time. Dr. L. from Sioux City, Iowa, enters the Hotel Mercur, one of the two hotels where the scientists are staying, and asks the hotel clerk, "Say, are you broadcasting the World Series on television?"

"I beg your pardon, sir. And what is the World Series?"

"A ball game."

"Egh."

"I was sure that it would be televised over here by satellite."

"I suggest, sir, that you forget your World Series and take in a sauna, complete with female masseurs, at the VIP Club on the Nygade."

Evening. The stately facades of downtown Copenhagen are awash with light. The Town Hall on Raadhus Pladsen is also lit in honor of the cancer scientists in town because the mayor is holding a reception for the scientists there. After a glowing speech from the mayor, the scientists are ushered into an immense ballroom filled with smorgasbords and beer. The regulars on the world cancer meeting circuit now have a chance, once again, to greet each other, to talk shop and even to broach more risqué subjects. To wit: Danish scientist Gunnar is chatting with French scientist Jean-Jacques. Says the latter: "Copenhagen is *terriblement* expensive, *n'est-ce-pas*? How do you ever afford it?"

Gunnar replies with a cool Scandinavian smile, "by getting as many free dinners at the Town Hall as possible."

Not far away, Dr. R. from Sioux City, Iowa, can be overheard saying, "Hey, there's my old friend Ivan from Moscow, the one with the peg leg. He was a fighter pilot in World War II. How are you doing, Ivan?"

Bushy eyebrows wiggling, blue eyes sparkling, Ivan clasps Dr. R. in a bear hug. "Not bad, Sam. Not bad at all."

"I hear one of our next meetings is going to be held in the Soviet Union. How are you going to entertain us?"

"With 150-proof vodka, moi droog."

Not all is smoked Limfjord mussels, capers and schnapps during the meeting, of course. The scientists have their serious discussions and moments, but even then

their humanness is frequently and beautifully obvious. Dr. T. from Tübingen, for example, can be seen laying an affectionate hand on the shoulder of a French scientist, one of the nicer things that has happened to French-German relations in a while. Dr. P. can be heard sympathizing on behalf of Dr. K.: "He is a terrific person. Unfortunately he has the thankless job of checking out one lab after another to see whether scientists' tissue cultures are contaminated with HeLa cells."

Then during the meeting George Klein of the Karolinska Institute in Stockholm announced that the Nobel Prize for medicine had just been awarded to Howard Temin, David Baltimore and Renato Dulbecco for their work on cancer viruses; specifically for work on the now famous enzyme, reverse transcriptase.

All eyes turned to a pretty, young virologist in bluejeans, Alice Huang. Alice is David Baltimore's wife. Overjoyed, she rushed from the room to phone her husband in the United States and to tell him the good news.

A little later, SCIENCE NEWS asked Alice whether she and David had been expecting him to receive the award. She replied with an impish smile, "Actually David and I have known that his name has been nominated for several years now. But some other scientists who have had their names nominated in the past have been terribly depressed when they did not win the prize. So David and I tried to not think about it, especially since David is only 38, and we did not expect them to give the prize to anyone so young."

But perhaps the nicest thing that has become apparent at this cancer meeting in Copenhagen is that cancer scientists are eager to find a cancer cure for more than just intellectual gratification alone. In other words, they too are touched in very personal ways by the tragedy of this ubiquitous killer.

For instance, Dr. D. from Chicago could be overheard saying to Dr. G. from New York City: "My sister died from hepatic carcinoma two months ago. We've got to find a cure for cancer, Bernie."

"I know," Bernie replies with a sigh, "and it sure as hell isn't easy."

—Joan Arehart-Treichel