Long-Term Follow-Up Study

UNIVERSITY OF MINNESOTA
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University of Minnesota
The Denver Children's Hospital
Children's Hospital of Pittsburgh
Children's Hospital at Stanford University
Dana-Farber Cancer Institute
Emory University School of Medicine
Children's National Medical Center
U.T.M.D. Anderson Cancer Center
Memorial Sloan Kettering Cancer Center
Texas Children's Hospital
University of California at San Francisco
Seattle Children's Hospital & Medical Center
Toronto Hospital for Sick Children
St. Jude Children's Research Hospital
Children's Hospital of Columbus
Roswell Park Cancer Institute
Mayo Clinic
Children's Health Care - Minneapolis
Children's Hospital of Philadelphia
St. Louis Children's Hospital
Children's Hospital of Los Angeles
UCLA Medical Center
Miller Children's Hospital
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Riley Hospital for Children-Indiana University
UAB/The Children's Hospital of Alabama
University of Michigan-Mott Children's Hospital
Children's Medical Center of Dallas

The Long-Term Follow-Up Study newsletter is written and published by the University of Minnesota Department of Pediatrics, Division of Pediatric Epidemiology & Clinical Research.

From the Editor

Welcome to the third edition of the Long-Term Follow-up Study newsletter. In this issue we feature an article on the role of genes in cancer and similar illnesses. We also provide you with some facts about an important health concern, hepatitis C.

This is a very exciting year for the Study, as we finish recruiting the members of our cohort (a term for the total group of participants in the study). Currently, over 13,650 people throughout the United States and Canada are participating in the Long-Term Follow-Up Study, and we have already begun to analyze the valuable information you have given us. Later this year we plan to begin publishing our findings and we will, of course, keep you informed when we do.

New smoking study

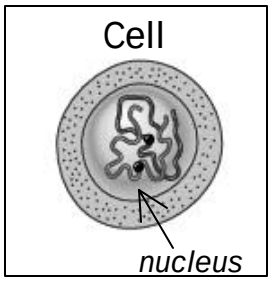
As we reported in last year's newsletter, about 28% of study participants over the age of 18 have smoked tobacco. Researchers at the Dana Farber Cancer Institute in Boston, together with the Long-Term Follow-Up Study team, have received a grant from the National Cancer Institute to look at the health practices (including smoking habits) of our study participants. In connection with this, some of you may receive brief phone calls from individuals with similar health backgrounds to talk about your health and health-related behaviors. Participants will be able to share their thoughts and concerns about either continuing to smoke or quitting smoking. If you are interested in providing your opinions and thoughts about health-related issues, please call Dr. Ann Mertens at 1-800-775-2167.

Genes and the fight against cancer

By participating in the Long-Term Follow-Up Study, you are making an important contribution to the fight against cancer, leukemia, and similar illnesses. The information you have already given us will help doctors and scientists in their efforts to create new and better treatments and to identify the health-related issues of having been successfully treated for one of these diseases.

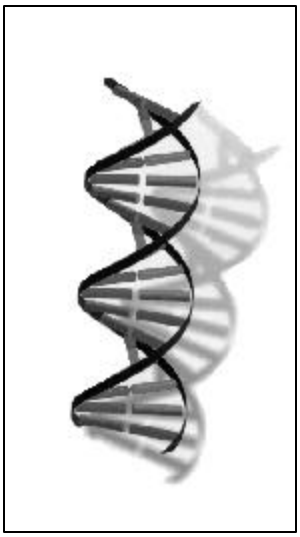
There are many causes of cancer, most of which are not known. What *is* known is that some genetic factors in people can make it more likely for them to develop cancer. By comparing the genetic material (DNA) from a great many people, scientists can gather clues about which genes might increase a person's risk.

Some facts about cells, genes, and DNA



Cells are the basic units of the human body, and of all living things. Our bodies are composed of brain cells, bone cells, blood cells, and other types of specialized cells that make up our organs, our muscles and all our other physical systems. The nucleus of each cell contains the genetic material that makes us unique.

Chromosomes. In the nucleus of each cell, genes are found on thread-like structures called chromosomes. Each cell (except for sperm and egg cells) has 46 chromosomes arranged in 23 pairs. We get one of each pair from our fathers and one from our mothers. Chromosomes are made of DNA and protein. The DNA is what carries our unique "genetic code", a blueprint for life.



DNA is a very long, tightly packed molecule made up of individual units, or building blocks, called nucleotides. The nucleotides are strung together in pairs on two long chains and it is this pairing that forms the DNA double helix. There are about three billion nucleotide pairs in each of our cells. Unless you have an identical twin, the pattern they are arranged in is unique to you.

Finally, a ***gene*** is a segment of a DNA molecule that contains instructions for the body to produce a particular protein. The protein then determines or helps to determine a physical trait. Humans have about 100,000 genes. Some genes produce noticeable traits, like hair or eye color. Others produce traits that can't be seen, like our blood type. Scientists believe that each person's unique genetic code also plays a part in shaping more complex traits, such as intelligence. And, it can influence our susceptibility or resistance to certain diseases, including cancer.

"Banking" DNA

In collaboration with the Long-Term Follow-Up Study, researchers at the University of Minnesota are planning to create a library, or bank, of DNA from survivors of cancer, leukemia and similar illnesses. DNA from this bank would be made available to scientists who are seeking to discover which genes might be involved in the development of cancer and similar diseases (and their complications). An example of how the Univer-

sity of Minnesota'a DNA bank will be used in the fight against cancer is the new research project led by Dr. Stella Davies, a pediatric oncologist at Minnesota. Dr. Davies' study will test whether people who lack certain genes (known as GSTM1 and GSTT1) have an increased chance of developing a second malignancy after receiving chemotherapy for cancer. The genes she is studying work to break down certain toxic agents in chemo-therapy drugs. They also help neutralize some cancer causing agents found in tobacco smoke. Dr. Davies plans to use samples from the DNA bank to find out how many people who develop second cancers are missing these genes. The results of her study could make it possible to screen future cancer patients and develop alternative treatments for those at risk.

As a member of the Long-Term Follow-Up Study cohort, you may be asked to donate some cells for the DNA bank. Cells can be collected very easily from the inside of the mouth by rinsing vigorously with a mouth-wash, such as Scope, for 30 to 60 seconds. If we ask you to donate cells for the DNA bank, we will send you a sample of mouthwash and a collection bottle to mail your cells back to us. Alternatively, if you had surgery to re-move a tumor, we may ask your permission to acquire some of the tumor tissue from the hospital where you had your surgery for storage in the bank.

As always, you have the right to decide whether or not to participate. If you *do* donate cells, they will be labeled only with a number--researchers who study your DNA will not know who you are. Your DNA will not be altered in any way or used for any purpose other than cancer research. Your participation in the DNA bank, like the other aspects of your participation in the Long-Term Follow-Up study, is totally confidential.

Literature Watch

In this section we review papers from medical and scientific journals that may be of interest to study parti-cipants.

Researchers at the St. James Hospital in the United Kingdom recently completed a study of dental health in individuals who had been treated for a malignant disease before the age of 10. The researchers compared these individuals to their brothers or sisters who were closest to their age. They found that, compared to their siblings, the individuals who had been treated for malignant disease had the same number of cavities, but more defects in the enamel that protects the teeth from decay. They also had more untreated cavities and more of them had severe gingivitis (gum disease) than their brothers and sisters, which suggests that they do not see a dentist as regularly as they should.

Editor's comment: This investigation from the U.K. points out something we all know, but often neglect: Dental care is an important part of our overall health. Unlike many facets of our lives, it is also something we can do something about and have a positive impact on our future health. Regular brushing, flossing, and especially regular trips to the dentist are critical, particularly if you have had radiation therapy to the head or neck. Certain chemotherapy drugs may also lead to poor enamal formation so keeping ahead of dental problems is the best plan of all.

"Dental parameters in the long term survivors of childhood cancer compared with siblings" can be found in: *Oral Oncology*, Vol. 33, No. 5, 1997, pages 348-353.

In a collaborative study from five countries - Denmark, Finland, Iceland, Norway, and Sweden - scientists studied the risk of cancer in the offspring of childhood cancer survivors who had been diagnosed before the age of 20. They found that the children of individuals who had been diagnosed with a type of cancer that is hereditary, such as some forms of retinoblastoma, were at high risk of developing cancer. However, the children of individuals who had been diagnosed with a non-inherited type of cancer showed no increased cancer risk.

***Editor's comment*:** In our last issue we discussed a study that reported no increase in risk of birth defects among children of survivors of acute lymphoblastic leukemia. This article covers another important issue, the risk of cancer in offspring of childhood cancer survivors. Results from this study are encouraging. In combination with similar findings by other studies, they support the conclusion that, except for the very few types of cancers that are known to be hereditary, most survivors do not "pass on" cancer to the next generation.

"Risk of cancer among offspring of childhood cancer survivors" can be found in: *The New England Journal of Medicine*, Vol. 338, 1998, pages 1339-1344.

What is HEPATITIS C?

Hepatitis is an inflammation of the liver. Hepatitis A and B are the best-known types. Others are called hepatitis non-A non-B (NANB). The most common type of hepatitis NANB is hepatitis C. This virus invades and destroys liver cells. The body can usually overcome the virus, but chronic (long-term) infection may occur. The following article is from the After Completion of Therapy (ACT) Clinic at St. Jude's Reserach Hospital, Melissa Hudson, M.D., director.

How does it start?

The hepatitis C virus is carried by the blood. Many infections are caused by needle sharing among drug users. Transfusions now cause fewer than 5% of hepatitis C infections. However, the blood supply was not routinely screened for hepatitis C before 1992. Anyone who received a blood transfusion before that time is at risk and should request a screening blood test from their family doctor or health-care provider. The virus can also be spread through other kinds of blood contact, hemodialysis, and organ transplantation. The infection may possibly be transmitted through sexual contact, and from mothers to infants before birth. In 40% of cases, the source of infection is not known.

How serious is hepatitis C?

The infection is usually short and mild. However, about half of patients continue to be infected even though they may feel well. Some develop serious long-term effects. About 20% of patients develop scarring of the liver (cirrhosis), and a very few develop liver cancer.

What are the signs of hepatitis?

A few weeks or months after infection, patients may feel tired, lose appetite, feel pain or tenderness in the abdomen, or have dark urine or yellowing of the skin and eyes. Many patients have no symptoms at all, but routine blood tests may reveal the infection. A positive test may mean acute (initial), chronic (long-term), or past infection. A few false positive tests are caused by other conditions. To know exactly what is wrong with you, your doctor needs other information in addition to this test. This test is not related to AIDS.

Preventing the spread of infection

If you should become infected, use the following precautions:

- ❒ Others should not use your razor, toothbrush, nail clippers, or any item that may come in contact with blood.
- ❒ Clothing, sheets, or towels with blood stains can be washed with the family laundry. Add one cup of bleach to the wash load.
- ❒ It's OK to share your silverware, glasses, and dishes. Casual kissing is not a problem. Urine and saliva are a danger only if they contain blood.
- ❒ It is not known if hepatitis C can be transmitted sexually, but about one-third of spouses married for 20 to 50 years become positive for the virus. Sexual intercourse should be avoided if there is any genital bleeding, such as menstrual periods, genital ulcers, or cuts. Routine condom use may be the wisest course for couples beginning a new sexual relationship.

What can be done about hepatitis C?

During the initial illness, treatment is given only for troublesome symptoms. Patients with symptoms of chronic hepatitis should ask their doctor if they are good candidates for long-term treatment programs. Antiviral therapy for hepatitis C is typically recommended only for patients with abnormalities of liver function. Anyone who tests positive for hepatitis C should be aware of other infections and health habits that are harmful to the liver. Immunization with hepatitis A and B vaccines (if you don't already have immunity) and abstinence from alcohol will protect the liver from further injury if you have chronic hepatitis.