

THE SEARCH CONTINUES.....

Thank you for taking part in the Clue II program in 1989, 1996 and again in 1998. When the Clue program began in 1974 we had no idea that it would continue for over 25 years. You and the other 32,897 participants have helped greatly in our continuing efforts to solve some of the puzzles of cancer and heart disease. Using serum samples and information from the Clue programs of 1974 and 1989, we have had over 50 papers published in medical journals. Some of the most exciting findings of the past year are:

- Postmenopausal women with low serum concentrations of vitamin B12 were at higher risk of developing breast cancer than women with high concentrations. To our knowledge this is one of the first studies to examine the association between serum levels of B-vitamins and breast cancer risk. It may be that an unidentified protective factor for breast cancer associated with higher B12 concentrations might have led to the observed protective association. These findings need to be repeated before recommendations can be made. B12 is found in animal foods, especially organ meats, eggs, milk, oysters and clams.
- A study was conducted to examine the association between serum concentrations of pesticides (DDT, PCB's) and the development of breast cancer. Results of the study are reassuring. After 20 years of follow-up, exposure to relatively high concentrations of pesticides showed no evidence of contributing to an increased risk of breast cancer.

The information you have provided has enabled us to continue this valuable research. We once again have carefully reviewed all the items that might be related to the development of disease, to find what information appears most promising in the near future. After much consultation, we have developed a new questionnaire to update previous information as well as to obtain additional information about diet, medication and supplement use, health screening practices and other risk factors for cancer and heart disease. This questionnaire will be mailed in the spring of 2000.

Again, we thank you for your help in solving some of the puzzles of cancer and heart disease. As we've said before, with your continued help more pieces will be tried, some will fit, and the goal will come closer. So when your questionnaire arrives, please spare a little more time to give us some more clues. Your contributions will make a tremendous difference, and we are grateful.

Our major research activities at present involve looking at the association between exposure to pesticides and the development of prostate cancer, and an examination of the combined effect of selenium and vitamin E in protecting against prostate cancer. We are also studying the effects of the interaction of genes and the environment on health. We hope to publish these findings in the near future.

LOOKING TOWARDS THE FUTURE:

Why is it that some people smoke all their lives and rarely have health problems and others get serious illness such as cancer or heart disease? Because we all react differently to environmental factors. These differences make us more or less susceptible to beneficial or harmful exposures in the environment. Some people may be better than others at removing harmful chemicals from the body or repairing damage the chemicals may have caused to the cell structures. The removal and repair processes are done by special proteins in the body called enzymes. We may differ in how much of the enzymes are made or how rapidly the enzymes work. One way to look at the differences in the proteins is to look at the DNA. DNA is the basic building block of life and makes up the genes that, in turn, determine how much and how well our body's enzymes may work. Natural variations in our gene structure lead to differences in protein activity. By studying how, if at all, these naturally occurring genetic variations relate to health outcomes, we can begin to learn how to modify our lifestyle such that our behavior can work better with our genetic makeup and we stay healthy.

We can look at these variations in the DNA because you gave us a blood sample and permission to store all the components of the blood. This includes white blood cells, which contain the DNA. We are looking at differ-

ences in the genes that code for enzymes that can process chemicals to be less harmful, repair damage to DNA or are involved in others ways to keep cells healthy. The genes that we are studying have variations that are usually present in 10 to 50 percent of the population. These common genetic differences are called genetic polymorphisms. Since we are just beginning these studies, we do not yet know if the genes or enzymes they produce are important in protecting us from getting cancer or other diseases. By building on the results of this study and others we hope we can get more clues on how the environment and our bodies work together to keep us well. Eventually we hope to find out who most needs help to prevent disease.

As with all of our studies, all information is kept confidential. Names are not kept with blood results. Records are kept in rooms that are locked when not in use and data in our computers are not accessible through outside telephone lines, thereby making it impossible for "hackers" to obtain access to our records. In over 35 years of doing research, confidentiality has never been breached. To make information even more secure, we are obtaining a Certificate of Confidentiality, which is issued by the National Cancer Institute as an added protection of privacy, such that persons in research will not be compelled to identify any research participants in Federal, State or local civil, criminal, administrative, legislative or other proceedings. This will give added protection to ensure that only individuals associated with our team will have access to the data. We are in the process of establishing a Community Advisory Group to review research protocols that involve

participants from the community, and promote community awareness of the importance of our research in improving the health of individuals. As always, if you have any questions, please feel free to call us.

NUTRITION AND CANCER "FIVE A DAY" FOR BETTER HEALTH

Cancer is currently the second leading cause of death for American adults. It is projected to be the number one cause of early death in the next century, in part because as people live longer the risk of getting cancer increases. Lifestyle is a critical factor in most forms of cancer. Although we have little control over our genetic risks for cancer, we do have a choice in deciding which lifestyle risks to take, especially with regard to diet, smoking, and alcohol intake. One-third of all cancers in the United States are associated with tobacco use. About half of all cancers of the mouth, pharynx, and larynx are associated with heavy use of alcohol. The American Cancer Society estimates that about one-third of cancer deaths in this country are due to dietary factors.

The Johns Hopkins Research Center has added a great deal to studies of diet and cancer. Research has suggested that people who eat diets with lots of fruits and vegetables have lower risks for some cancers than people who eat few of these foods. Some evidence suggests that vegetables may protect against colon and rectal cancer because of the anti-oxidant compounds they contain, or their fiber content. Studies have also suggested that fruit and vegetable consumption also decrease breast and lung cancer risk because they contain protective plant chemicals called phytochemicals. Research has suggest-

ed that lycopene, the compound found in tomatoes that makes them red, may lower the risk of prostate cancer. Lycopene is best absorbed by the body when tomatoes are cooked; tomato paste and sauce are good sources of this substance.

"Five A Day" is a national effort to encourage us to eat at least 5 servings of fruits and vegetables everyday. Sponsored by the National Cancer Institute, this message is based on research that indicated that healthy eating starts with at least 2 servings of fruits and 3 servings of vegetables everyday. Fruits and vegetables are naturally low in calories and fat, and provide fiber, vitamins and minerals. Nutritionists recommend eating a variety of fruits and vegetables, rather than relying on vitamin and mineral supplements to help protect yourself against cancer. Research studies also suggest that eating fruits and vegetables are better than relying on supplements.

A serving is:

- 1 medium fruit
- 1 cup of leafy vegetables
- ½ cup of cut-up fruit or vegetables or cooked vegetables
- ¼ cup dried fruit
- ½ cup cooked beans or peas
- ¾ cup 100% juice

Results of the 1998 Clue II follow-up questionnaire found that 15 percent of men and 22 percent of the women, who responded to the questionnaire, eat 5 or more servings of fruits or vegetables a day. This important information will allow us to make comparisons of the health of persons with high and low fruit and vegetable intake. It's easy to add 2 servings of fruits and vegetables a day. Add a low-fat salad to lunch and crunch on an apple for a snack. Take a minute during the day and count

up how many fruits and vegetables you've had. Then you can plan for the other servings during the rest of the day. If some kinds of fruits and vegetables are healthier than others, we hope to find this out.

We can't control some factors related to our risk of getting cancer, such as a genetic predisposition, but diet is important and is under our control. Why not start now, when fruits and vegetables are plentiful, to take the Five a Day Challenge?

SELENIUM, VITAMIN E AND PROSTATE CANCER

Selenium is an essential trace mineral found in the soil. The selenium content of food varies with the concentration present in the soil. It is found in grain products, meats, eggs and shellfish. Selenium is an anti-oxidant and interacts with vitamin E which also functions as an anti-oxidant and is found most abundantly in plant oils. Together they protect cells against free radical (oxidizing) compounds. Free radicals are highly reactive compounds containing an unpaired electron when formed within cells, then cause damage and are believed to be associated with the development of disease. Free radicals seek electrons by attacking other compounds. One reason that free radicals are destructive to cells is that they can set off a

chain reaction in which thousands of free radicals are generated within minutes starting from a single one. Vitamin E can stop such chain reactions and help prevent cell destruction. Vitamin E and selenium work together to protect cells against cell damage due to free radicals. Studies are underway to help clarify the combined effect of selenium and vitamin E against cancer.

A number of epidemiologic studies have found that higher blood concentrations of selenium are associated with a reduced risk of cancer. In one study among Finnish smokers, there was no association of selenium intake with subsequent prostate cancer among the groups not given vitamin E; however, among those given vitamin E, higher intakes of selenium were associated with a slightly reduced risk of prostate cancer. Selenium was not found to be effective in preventing the recurrence of skin cancers in one study. However persons taking the selenium had fewer cases of cancers of the lung, colon and rectum, and prostate, with the strongest and most significant protection being against prostate cancer. Shortly after the report of this study, another study among health professionals also found a reduced risk of prostate cancer associated with higher concentrations of selenium in toenail clippings.

Food Sources of Selenium

| Food item and amount | Selenium (micrograms) |
|-------------------------|--------------------------|
| Canned tuna, 3 oz | 68 |
| Sirloin steak, 5 oz | 48 |
| Shrimp, 4 oz | 45 |
| Cooked egg | |
| noodles, 1 cup | 35 |
| Roasted ham, 3 oz | 30 |
| Roasted chicken, 3 oz | 24 |
| Boiled egg, 1 | 11 |
| Whole-wheat bread | |
| 1 slice | 10 |
| Oatmeal, ½ cup | 10 |
| White bread, 1 slice | 8 |

Food Sources of Vitamin E

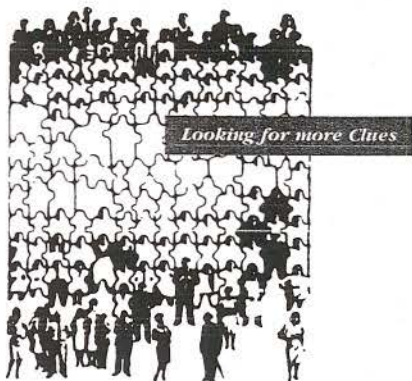
| Food item and amount | Vitamin E (IU) |
|-------------------------|-------------------|
| Sunflower | 21 |
| seeds, 1 oz. | |
| Sunflower oil, | |
| 1 tbsp | 10 |
| Almonds, 1 oz. | 10 |
| Safflower oil, 1 tbsp | 9 |
| Wheat germ, | |
| ¼ cup | 8 |
| Peanut butter, | |
| 2 tbsp | 5 |
| Mayonnaise, 1 tbsp | 1 |

In order to further investigate these findings, researchers at the Johns Hopkins Research Center have recently completed a study looking at the association of selenium in toenail clippings and vitamin E levels in the blood. In addition to the toenail and blood samples, we are also using the questionnaire information that you have provided in 1989 and during the past 3 years.

Findings from this study showed that persons with high levels of one kind of vitamin E (gamma-tocopherol) in the blood were associated with lower risk of prostate cancer, especially if these persons also had high levels of selenium. The major source of gamma-tocopherol is the diet; vitamin E supplements usually do not contain this form of vitamin E. This finding appears to be an important clue. However, like all studies among human beings, and contrary to most media stories, a single study should never be accepted as proof. If this clue is confirmed by others, then we can be reasonably certain that it fits the puzzle of prostate cancer. For the present, it is important to keep in mind that our diets can provide many essential food elements that cannot be put into pills.

GINKGO BILOBA RESEARCH STUDY

Washington County has been selected by the National Institute of Health as one of three sites to study the effects of the widely used herb, ginkgo biloba, in preventing or delaying changes in memory, mental alertness, and personality, that can occur in people as they get older. Ginkgo biloba (also known as the Maidenhair Tree) is derived from the leaves of one of the world's oldest surviving tree species, believed to have originated over 200 million years ago. Ginkgo



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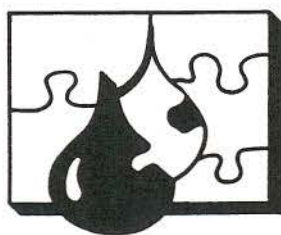
trees are tall hardy trees with distinctive fan-shaped leaves. Ginkgo is considered a sacred tree by the Chinese, with medicinal use dating to ancient times.

The Cardiovascular Health Study (CHS) in Hagerstown, which is managed by Johns Hopkins University, is one of the sites funded to conduct the clinical trial. CHS is recruiting 750

men and women 75 years of age or older, who are residents of Washington County, and able to come to the CHS clinic downtown, to participate in the study. Other eligibility criteria may also apply, but will be discussed at the time of application.

We invite you to help with this important new study which will enable us to determine the value

of Ginkgo biloba in the prevention of dementia, or in the delay of onset, or progression of memory loss. If you are interested in participating, please call Pat Crowley at the CHS office (301-733-8860) between the hours of 9 AM and 4 PM, and ask for the Ginkgo Biloba Trial. Participation in this study will contribute greatly to the public health.



**OPERATION
CLUE II**

Give Us A Clue

Campaign Against Cancer and Heart Disease