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New technology for cancer detection

The new NMR technique seems to be on the way to becoming a reliable test to detect the presence of cancers.

Medical scientists have long sought a blood test to detect the presence of cancer. During this time, a number of different chemicals have been found to be associated with particular tumors and have been utilized primarily to evaluate the treatment and management of already diagnosed cancers.

In the Nov. 27, 1986 *New England Journal of Medicine*, scientists at the Charles A. Dana Research Institute, Beth Israel Hospital, and the Harvard Medical School, report on the detection of malignant tumors of various types by use of a technique called water-suppressed proton nuclear magnetic resonance (NMR) spectroscopy of plasma.

Unlike other blood tests, such as carcinoembryonic antigen, beta-human chorionic gonadotropin, and alpha-fetoprotein which measure the presence of chemicals produced by specific tumors, this technique appears to measure the body's response to the presence of cancer of any type and to clearly discriminate between cancer-bearing and non-cancer-bearing patients.

Proton NMR is a technique for determining the degree of order of cells or molecules. This is done by polarizing hydrogen atoms (protons) in a strong magnetic field and then measuring the amount of time required for them to resume their normal positions. This "relaxation time" is correlated to the degree of organization of the molecules in question. Highly organized molecules, and healthy cells, rapidly return to their resting state, whereas less ordered molecules, and diseased cells such as cancer, relax much more slowly.

The use of NMR to detect cancer was first proposed in 1971 by Dr. R. Damadian, who pioneered the development of large NMR scanners capable of scanning an entire body and detecting cancers in a manner analogous to CAT scanners, but with much better resolution. This work has been expanded by other workers, such as Dr. James Frazer in Texas, who have used variations on this technique to not only detect, but also treat some cancers.

The high cost, and limited availability of NMR scanners, have so far precluded the use of NMR as a screening test. However the technique developed at Harvard uses a smaller instrument to analyze a sample of blood plasma, rather than a whole patient.

Researchers had noticed increased relaxation times in the serum and uninvolved organs of animals with malignant tumors, as well as small but statistically significant increases in the serum of patients with malignant tumors. These differences were small and did not distinguish between benign and malignant tumors. They were useless for diagnosis or prognosis.

Since the relaxation time of plasma is a composite of the protons of water and various other molecules in the plasma, the researchers decided to examine NMR spectra of protons other than water in the plasma of patients with cancer and in the plasma of control groups. They did this by utilizing the capability of modern NMR spectrometers to suppress the resonance of water protons. This leaves mainly the spectrum of plasma lipoproteins (combinations of fat and protein) as well as a number of small molecules which are present in high concentrations.

Sorting through these different spectra, they settled on the methyl and methylene groups of the lipids of the plasma lipoproteins as the variable of interest. They looked at these spectra in 331 patients. These consisted of patients with untreated cancers, currently or previously undergoing treatment for cancer, with benign tumors, pregnant women, and two control groups.

The results showed that this technique reliably distinguished patients with malignant cancers from normal controls and patients with non-cancerous disease, as well as patients with benign tumors. However, pregnant patients and patients with benign prostatic hyperplasia had readings consistent with the presence of malignant tumors. The prostatic hyperplasia cases may indeed have had undetected cancers, not that uncommon in such patients and often detected at autopsy after the patient has died from some other cause.

The reactions in the pregnant women are interesting. They indicate that what is being detected is a reaction on the part of the host to the growth and not a tumor product.

These preliminary results indicate that water-suppressed proton NMR spectroscopy of plasma may indeed provide us with a highly accurate test to detect many different cancers. What is more significant are the potential breakthroughs in our understanding of the general phenomena of cancer as a disease process. It is in the area of the spectral analysis of living systems and not in the linear reductionist approach of molecular biology that we will make the fundamental breakthroughs necessary to conquer cancer, AIDS, and aging.

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