

From dusty punch cards, new insights into link between cholesterol and heart disease

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John Gofman initiated studies that led to the understanding of the effects of lipoproteins on cardiovascular disease. His research is still yielding insights today.

(PhysOrg.com) -- A stack of punch cards from a landmark study published in 1966, and the legwork to track down the study's participants years later, has yielded the longest analysis of the effects of lipoproteins on coronary heart disease.

The study, published in a recent issue of the journal *Atherosclerosis*,

tracked almost 1,900 people over a 29-year period, which is nearly three times longer than other studies that examine the link between different sizes of high-density lipoprotein particles and heart disease.

It found that an increase in larger high-density lipoprotein particles decreased a subject's risk of heart disease. The research also underscores the value of looking to the past to advance science.

"Often we think only of designing new studies with the latest technologies, but there are treasures buried in our past," says study author Paul Williams of the U.S. Department of Energy's Lawrence Berkeley National Laboratory.

Lipoproteins are fat molecules that carry cholesterol in the blood. Cholesterol is divided into high-density lipoprotein, the so-called good cholesterol, and low-density lipoprotein, the bad cholesterol.

That's common knowledge today. But it was a groundbreaking and controversial notion in the 1950s, when Berkeley Lab's John Gofman used an analytic ultracentrifuge at Berkeley Lab to separate and measure the different lipoproteins. He was the first to propose that high-density and low-density lipoprotein particles play a role in heart disease.

His research was met with skepticism, however, so Gofman began a prospective study of lipoproteins in a group of 1,905 employees at Lawrence Livermore National Laboratory between 1954 and 1956. After ten years, there were 38 new cases of heart disease. In 1966, he reported that men who developed heart disease had lower levels of the HDL2 (the larger high-density lipoprotein particles) and HDL3 (the smaller high-density lipoprotein particles).

It would take several more years for Gofman's work to gain currency in the scientific community. Gofman left lipoprotein research in the 1960s

to pioneer the study of the biological effects of low doses of radiation. He died in 2007.

His Livermore cohort study collected dust until 1988, when Williams discovered the study's punch cards at the University of California, Berkeley's Donner Hall. Realizing he had found an epidemiological goldmine, Williams verified the cards' authenticity by examining logbooks. He also found an old punch card machine to extract their data. Then, with the help of students and research assistants, he located and contacted 97 percent of the people in Gofman's study over the next nine years.

"Often, all we had to go on was an address on a street that no longer existed," says Williams, a staff scientist in Berkeley Lab's Life Sciences Division. "Women had changed their names, employees had left or retired and moved, and many had died. However, by telephoning neighbors and coworkers, we were able to track down all but a few."

Medical records were obtained and reviewed by a physician, Daniel Feldman, who is the study's co-author.

Their 29-year follow-up uncovered 363 cases of coronary heart disease. They found that both HDL2 and HDL3 lowered heart disease risk, and that a one-milligram per milliliter increase in HDL2 produced a significantly larger reduction in [coronary heart disease](#) risk than a one-milligram per milliliter increase in HDL3. Their follow-up also buttressed Gofman's insights from 1966.

"Gofman's original conclusion that ischemic heart disease is inversely related to both HDL2 and HDL3 was upheld in the current analyses," says Williams, who hopes to complete the 55-year follow-up of this cohort.

The research was funded with grants from the American Heart Association and the National Institutes of Health's National Institute on Aging.

More information:

- Williams' study, "Prospective study of coronary heart disease vs. HDL2, HDL3, and other lipoproteins in Gofman's Livermore Cohort," was published online Oct. 23, 2010, in the journal *Atherosclerosis*.
- Gofman's 1966 study, "Ischemic heart disease, atherosclerosis and longevity" was published in the journal *Circulation*, 1966;34:679-697

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