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Biomedical Research on Hypercholesterolemia

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ELL

About 20 years ago, before I was born, my great grandmother died a sudden death, most likely from a heart attack. She was only 62 years old. Coronary heart disease has been and still is responsible for more than 30% of the deaths in the Western World.

Ten years later my grandmother participated in a cohort study in Tromsø (Norway). She volunteered to give blood samples and several different biological markers were measured. She had far too high levels of cholesterol and she was later diagnosed to have hypercholesterolemia, a hereditary disease that is life threatening if not treated.

Biomedical research has through experimental, genetic, epidemiologic and therapeutic investigation for the past hundred years established connection between Cholesterol and atherosclerosis but there are still lots of unknown in the disease of atherosclerosis.

As late as 1910, the German chemist Adolph Windaus found out that atherosclerosis plaque from human aortas contained 20 to 26 times higher levels of cholesterol than normal aortas. Between 1950 and 1960 scientists from the area of organic chemistry and enzymology determined how cholesterol was produced in the body. It turned out to be a complex pathway of more than 30 different steps.

We now know that Cholesterol is a substance no humans can live without. Cholesterol is an important part in a human cellular membrane. Not all Cholesterol is considered bad for your body. Cholesterol can be categorized due to their carrier protein; a bad one called low density lipoproteins or LDL and a good one called high density lipoproteins or HDL. Since cholesterol cannot mix with water it needs LDL or HDL to be transported in the bloodstream.

An epidemiologic study in 1955 by John Gofman, USA showed an association between levels of cholesterol, heart attacks and LDL. He also found that heart attacks were less frequent at higher levels of HDL in the bloodstream. Too much LDL cholesterol in the bloodstream can slowly deposit on the walls of the arteries, then form plaque and narrow the

blood vessels, leading to atherosclerosis and possibly coronary heart disease. HDL carries less cholesterol than LDL, but will help remove cholesterol by transporting it to the liver.

There are mainly two ways to get elevated levels of LDL cholesterol in the bloodstream. The most common is through nutrients, for example; butter, coconut oil and whole milk. In 1938 a Norwegian clinician Carl Müller described the genetic connection between cholesterol and heart attacks from several families which had inherited high blood cholesterols and premature heart attacks. This was later called familial hypercholesterolemia or FH. HDL can be increased with exercise, cessation of smoking and weight reduction.

Joseph L. Goldstein and Michael S. Brown shared the Nobel Prize in 1985 for their research on cholesterol metabolism and they were also the ones behind the discovery of the LDL receptor which is responsible for binding LDL to cells so that cholesterol can be used in the cell for metabolic purposes.

In 1986 the first drug that would selectively lower LDL without lowering HDL was approved and today several million people use this drug is called Lapaquistat. It has been clinicaltrils done on Lapaquistat Alone or Combined With High-Dose Statin, this was done from November 4, 2005 to January 13, 2009, people that were participating had to be 18 years and older. In 1994 researchers showed that this drug lowered LDL levels, prevented myocardial infarctions and generally prolonged life. Heterozygous or heritage only from one parent FH occurs in 1 out of 500 people in most countries, but Homozygous or heritage from both parents only occurs in 1 in a million births.

In one animal research they lowered LDL-cholesterol in rats by giving them either a drug that prevents the liver from secreting lipoproteins, or a drug that increases their disappearance. In both models, injection of endotoxin was followed by a much higher mortality in the low-cholesterol rats compared with normal rats.

Reflection

I chose this topic because my grandmother has hypercholesterolemia and I wanted to learn more about her disease. I also wanted to know if anyone else in my family has it. I and didn't know anything about my great grandmother and I have never met her before, so I wanted to know what she died of.

I wanted to know about the disease my grandmother has hypercholesterolemia and it was hereditary. I never talked about my grandmothers medicines with her and she told me that she does use medicine, but I still wanted to know about other treatments she was having. Most of all I wanted to know about the disease because I never talked to her about it. Now I know that it is hereditary hypercholesterolemia.

In the beginning my grandmother tried to eat healthier, but that didn't help very much since she has FH. She has a low number of LDL receptors, decreased ability to remove LDL and increased production of LDL, because she has inherited a mutant gene. Luckily for my grandmother the achievement of many biomedical researchers have led to not only the discovery of her disease, but also a life prolonging treatment.

Work cited

Goldstein JL, Brown MS "the LDL receptor." *Arteriosclerosis, Thrombosis and Vascular Biology*.2009; 29:431.

Smith, Pål. "Cholesterol – What now?" *The Journal of the Norwegian Medical Association* nr 9, 2001; 121:1022.

Jie Jack Li. "Triumph of the heart. The story of statins." Oxford University press 2009: 3-24.

"About mortality rates from heart disease" World Health Organization. 2010. World Health Organization. 21 Feb. 2010. <<http://apps.who.int/whosis/database/mort/table1.cfm>>.

Gunn Irene Iversen, retired banker, Tromsø, Norway. Personal interview; detection of disease and living with it. 15 Feb. 2010.