Fatal cholesterol disease overlooked and untreated

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Hereditary high blood cholesterol leads to premature heart disease. It is overlooked and untreated virtually worldwide—including in Europe. This is a major problem as the disease is dangerous for health. However, this disease is easy to diagnose and treat, according to the conclusion of a consensus report from the European Atherosclerosis Society. The report was recently published in the recognised medical journal *European Heart Journal*.

A new consensus report documents massive underdiagnosis and undertreatment of hereditary high blood cholesterol—so-called familial hypercholesterolaemia—in practically all 200 countries in the world, the only exceptions being the Netherlands and Norway.

"In most countries, the number of people with familial hypercholesterolaemia is unknown. This means that the condition is not detected until the person develops heart disease or dies suddenly far too young. Considering how easily the disease can be prevented, this situation is an admission of failure from a health perspective," says Børge Nordestgaard, Clinical Professor at the Faculty of Health and Medical Sciences, University of Copenhagen, and Chief Physician at Copenhagen University Hospital. He is the leading author of the new consensus report, which has been published in the *European Heart Journal*.

"In the general population, between 1 in 200 and 1 in 500 people inherit the disease familial hypercholesterolaemia, making the disease the most

frequent hereditary and fatal disease. However, statins, which are safe and inexpensive treatments, can lower cholesterol levels. For these persons with a greatly increased risk of developing serious heart disease, the few side effects associated with statins are negligible," says Børge Nordestgaard.

Between 14 and 34 million people worldwide are estimated to suffer from familial hypercholesterolaemia. In Europe, the number is between 1.8 and 4.5 million and, in Denmark, between 11,000 and 28,000. These figures are based on the large Copenhagen General Population Study.

"In the Netherlands and Norway, most people suffering from familial hypercholesterolaemia have been identified, and are offered cholesterol-lowering treatment with statins. In Denmark, only an estimated 500 persons with familial hypercholesterolaemia have been identified and undergone sufficient treatment," Børge Nordestgaard.

Easy to diagnose

Familial hypercholesterolaemia is easy to diagnose; it only requires a blood cholesterol test and a family history of early-onset heart disease. Cholesterol levels above 8 mmol/L in adults and above 6 mmol/L in children are a strong indication of the condition, and the diagnosis can be confirmed by a gene test.

"It is surprising and sad that even rich countries with highly developed health systems fail to help these people. It is not a question of economic resources, as the disease is easy to diagnose and inexpensive to treat," says Professor John Chapman. He is one of the co-authors of the report and Professor at the Pitié-Salpêtrière university hospital in Paris.

Coordinated national effort required

According to Børge Nordestgaard, a coordinated national effort is required, with clinics at all major hospitals in most countries, similar to the existing diabetes clinics.

"It would also improve the registration of familial hypercholesterolaemia and the families affected if the WHO decided to assign the disease its own diagnostic code as is the case with diabetes," Børge Nordestgaard concludes.

Facts

Familial hypercholesterolaemia may be caused by mutations (genetic defects) in three proteins, all of which play a role in the removal of cholesterol particles from the blood by the liver. These mutations affect the liver's LDL receptor. This receptor helps to control levels of LDL (low-density lipoprotein), the fat particle that transports most of the cholesterol in the blood.

Heterozygous familial hypercholesterolaemia means that the person has inherited one genetic defect from one of his or her parents. In Europe, between 1.8 and 4.5 million people have the heterozygous form of the condition.

Homozygous familial hypercholesterolaemia means that the person has inherited two genetic defects, i.e. one from each of his or her parents. In Europe, with a population of 900 million individuals, between 900 and 5600 children have been born with the homozygous form of the condition. However, many of these children are probably already deceased, since they were never identified in time to receive any treatment.

People with familial hypercholesterolaemia have high blood cholesterol throughout their life. If left untreated, they run a very high risk of heart

disease and premature death. If the condition is not treated, men and women with one genetic defect will typically have a cholesterol level of 8-15 mmol/L and will therefore most likely develop heart disease before the age of 55 and 60 years, respectively. The very unfortunate people who have inherited two genetic defects will have a cholesterol level of 12-30 mmol/L and will untreated develop heart disease and die before the age of 20.

Familial hypercholesterolaemia is primarily treated with statins and a cholesterol-lowering diet. If cholesterol levels are not lowered sufficiently, the cholesterol absorption inhibitor ezetimibe may be administered. The people with the highest blood cholesterol levels, those suffering from homozygous familial hypercholesterolaemia, are additionally treated with LDL cholesterol apheresis, a procedure similar to kidney dialysis.

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