HoFH UNCOVERED

living with extreme levels of cholesterol

Homozygous Familial Hypercholesterolaemia (HoFH) A RARE, LIFE-LIMITING CONDITION

GENETIC

It is genetic: Children inherit HoFH from both their parents.

ULTRA-RARE

It is ultra-rare: Estimated ~1.5 HoFH patients per million of population may be clinically diagnosed, with many more in some countries, either due to the gene pool or the number of marriages within families.[1]

EXTREME

10x

Arteries become clogged: People with HoFH often have 10 times the target level of cholesterol in their blood.[2]

LIFE THREATENING

Inevitably leading to severe heart disease: People with HoFH have an average life expectancy of just 45 years, more than 30 years shorter than the European average of 82.[3]

References: **1** Sjouke B et al. Homozygous autosomal dominant hypercholesterolemia in the Netherlands: prevalence, genotype-phenotype relationship and clinical outcome. European Heart Journal Advance Access (February 2014). **2** Raal FJ et al. Homozygous familial hypercholesterolemia: current perspectives on diagnosis and treatment. Atherosclerosis 223 (2012) 202-268. **3** Borberg H. 26 years of LDL – Apheresis: a review of experience. Transfusion and Apheresis Science 41 (2009) 49-59. **4** Horton JD et al. PCSK9: a convertase that coordinates LDL catabolism. Journal of Lipid Research (2009) 50: S172–S177. **5** Graesdal A et al. Apheresis in homozygous familial hypercholesterolemia: the results of a follow-up of all Norwegian patients with homozygous familial hypercholesterolemia. Journal of Clinical Lipidology (2012) 6, 331-229.

CHALLENGING TO LIVE WITH

VAST BUILD UP OF CHOLESTEROL

The liver of an HoFH patient cannot remove cholesterol from the bloodstream.

This leads to a rapid build up of unused cholesterol that deposits throughout the body under the skin, in tendons and most importantly in blood vessels, including of the heart.

CHILDREN EXPOSED TO AS MUCH CHOLESTEROL AS A 70 YEAR OLD

Left untreated, by the time children with HoFH are ~12 years old, they will likely have reached their cholesterol exposure for cardiovascular disease.

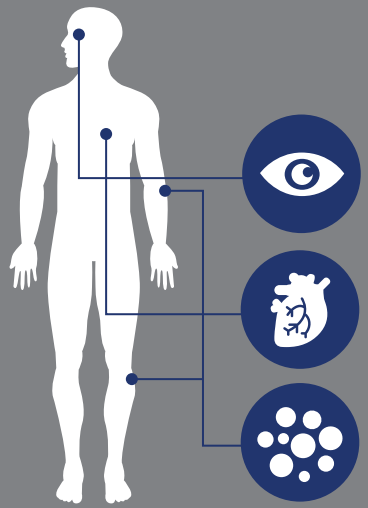
This normally would not happen until a person was 60-70 years old.[4]

Children who reach this threshold have an early and severe risk of heart attacks, strokes, major heart disease and premature death, often in the first decade of their life.

IMPACT ON LIVING LIFE

Patients with HoFH, undergoing treatments such as apheresis, often struggle to live their lives to the full because of a reduced ability to attend school and to work full-time, limiting their educational progress and employment options.

AFFECTS MULTIPLE ORGANS



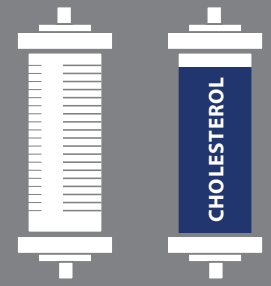
The physical signs of HoFH vary from person to person.

EYES: A whitish ring around the cornea (the clear outmost layer of the eye), known as arcus cornealis.

HEART: Chest pain, shortness of breath, or fatigue, which may be early signs of heart disease.

SKIN: Yellowish spots or bumps on the body (xanthomas) or around the eyes (xanthelasma).

HoFH IS HARD TO TREAT



Most treatments for HoFH, such as statins, ezetimibe and PCSK9 inhibitors aim to reduce the level of cholesterol in the body by increasing the rate of clearance. But these approaches rarely get patients to target levels. Apheresis is a common option. Blood is passed through a machine which filters cholesterol and removes it into a container for disposal (see graphic) but levels rapidly rebound to pre-treatment levels.

Apheresis is typically needed multiple times per week to be sufficient to control the disease.

However it is often only delivered once a week or once every two weeks, not enough to reduce cholesterol levels to the recommended targets. Available treatments have limited effect and heart disease still progresses.[5]

AMRYT PHARMA

References: **1** Sjouke B et al. Homozygous autosomal dominant hypercholesterolemia in the Netherlands: prevalence, genotype-phenotype relationship and clinical outcome. European Heart Journal Advance Access (February 2014). **2** Raal FJ et al. Homozygous familial hypercholesterolemia: current perspectives on diagnosis and treatment. Atherosclerosis 223 (2012) 202-268. **3** Borberg H. 26 years of LDL – Apheresis: a review of experience. Transfusion and Apheresis Science 41 (2009) 49-59. **4** Horton JD et al. PCSK9: a convertase that coordinates LDL catabolism. Journal of Lipid Research (2009) 50: S172–S177. **5** Graesdal A et al. Apheresis in homozygous familial hypercholesterolemia: the results of a follow-up of all Norwegian patients with homozygous familial hypercholesterolemia. Journal of Clinical Lipidology (2012) 6, 331-229.