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Super-sticky 'ultra-bad' cholesterol revealed in people at high risk of heart disease

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Scientists from the University of Warwick have discovered why a newly found form of cholesterol seems to be 'ultra-bad', leading to increased risk of heart disease. The discovery could lead to new treatments to prevent heart disease particularly in people with type 2 diabetes and the elderly.

The research, funded by the British Heart Foundation (BHF), found that 'ultrabad' cholesterol, called MGmin-low-density lipoprotein (LDL), which is more common in people with type 2 diabetes and the elderly, appears to be 'stickier' than normal LDL. This makes it more likely to attach to the walls of arteries. When LDL attaches to artery walls it helps form the dangerous 'fatty' plaques' that cause coronary heart disease (CHD).

CHD is the condition behind heart attacks, claiming 88,000 lives in the UK every year (1).

The researchers made the discovery by creating human MGmin-LDL in the laboratory, then studying its characteristics and interactions with other important molecules in the body.

They found that MGmin-LDL is created by the addition of sugar groups to 'normal' LDL – a process called glycation – making LDL smaller and denser. By changing its shape, the sugar groups expose new regions on the surface of the LDL. These exposed regions are more likely to stick to artery walls, helping to build fatty plaques. As fatty plaques grow they

narrow arteries - reducing blood flow - and they can eventually rupture, triggering a blood clot that causes a heart attack or stroke.

The discovery might also explain why metformin, a widely prescribed type 2 diabetes drug, seems to lead to reduced heart disease risk. Metformin is known to lower blood sugar levels, and this new research shows it may reduce the risk of CHD by blocking the transformation of normal LDL to the more 'sticky' MGmin-LDL.

Dr Naila Rabbani, Associate Professor of Experimental Systems Biology at Warwick Medical School, who led the study, said:

"We're excited to see our research leading to a greater understanding of this type of cholesterol, which seems to contribute to heart disease in diabetics and elderly people. Type 2 diabetes is a big issue – of the 2.6 million diabetics in the UK, around 90 per cent have type 2. It's also particularly common in lower income groups and South Asian communities. (2, 3)

"The next challenge is to tackle this more dangerous type of cholesterol with treatments that could help neutralise its harmful effects on patients' arteries."

Dr Shannon Amoils, Research Advisor at the BHF, which funded the study, said:

"We've known for a long time that people with diabetes are at greater risk of heart attack and stroke. There is still more work to be done to untangle why this is the case, but this study is an important step in the right direction.

"This study shows how the make-up and the shape of a type of LDL cholesterol found in diabetics could make it more harmful than other

types of LDL. The findings provide one possible explanation for the increased risk of coronary heart disease in people with diabetes.

"Understanding exactly how 'ultrabad' LDL damages arteries is crucial, as this knowledge could help develop new anti-cholesterol treatments for patients."

The research was published in the journal *Diabetes*.

More information:

1. Scarborough P et al (2010). Coronary heart disease statistics 2010 edition. British Heart Foundation: London.

2 Diabetes UK (2010). Diabetes in the UK: Key statistics on diabetes. Online at www.diabetes.org.uk/Documents/ … s_in_the_UK_2010.pdf

3. Department of Health (2007). About diabetes. Online at www.dh.gov.uk/en/Healthcare/Na … s/Diabetes/DH_074762

4. Research published in Diabetes online 27/05/11: 'Glycation of low density lipoprotein by methylglyoxal increases atherogenicity – a possible contributor to increased risk of cardiovascular disease in diabetes'. DOI 10.2337/db11-0085

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