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Atherosclerotic Plaques Form During a Late and Limited Time Period in Life, Atom Bomb Residues Reveal

In a new study performed in humans, researchers from Sweden's Karolinska Institutet have determined the age of atherosclerotic plaques by taking advantage of Carbon-14 (14C) residues in the atmosphere, prevailing after the extensive atomic bomb tests in the 1950s and 60s. The findings, published in the scientific online journal PLoS ONE, suggest that in most people plaque formation occurs during a relatively short and late time period in life of 3-5 years.

The investigators collected carotid plaques during carotid stenosis surgery at the Stockholm South General Hospital (Södersjukhuset). The patients were admitted for surgery since their carotid lesions partly obstructed the blood flow to the brain, causing symptoms of insufficient oxygen called Trans Ischemic Attacks (TIA) that in some cases also had lead to strokes.

The plaques were carbon dated at Uppsala University, by using Accelerator Mass Spectrometry (AMS). As a result of the extensive atomic bomb test in the 1950s and 60s, the atmospheric concentration of $14^{0}C$ rapidly increased. Since then the concentration of $14^{0}C$ is declining, which now can be used to determine the time of synthesis of any biological sample.

"We suspected that the plaque would be substantially younger than the patients, who were on average were 68 years old at surgery, but we were surprised when we found that the average age of these plaques was less than 10 years," says Associate Professor Johan Björkegren, who lead the study at the Department of Medical Biochemistry and Biophysics.

Another striking finding was that the variation of plaque age was low, suggesting that in most people plaque formation occurs during a relative short and late time span in life (3-5 years). If proven true, the growth of atherosclerotic lesions may be interrupted to prevent clinical manifestation, like TIA and stroke, even in late stages of life, at 60 years of age or possibly later.

During the last years, a number of $14^{0}C$ dating studies have been performed at Karolinska Institutet, revealing new perspectives on common diseases involving, fat cells, neurons and cardiomyopathies. However, unlike previous studies, the current study did not date DNA reflecting cell turn over, but instead the entire atherosclerotic lesion.

The age of plaques was also found to be associated to blood levels of insulin, and plaques with lower age (formed more recently) were found to be more unstable than older plaques and therefore more likely to cause clinical complications.

"The correlation between low plaque age, higher insulin levels and instability is also consistent with our findings of gene activity where younger plaques were characterized with higher activity of genes related to immune responses and oxidative phosphorylation," says Dr. Björkegren. "However, our study is small and need to be replicated in future, larger clinical studies before we can determine the exact roles of biological age for plaque stability and associated clinical events."

Journal Reference: 1. Sara Hägg, Mehran Salehpour, Peri Noori, Jesper Lundström, Göran Possnert, Rabbe Takolander, Peter Konrad, Stefan Rosfors, Arno Ruusalepp, Josefin Skogsberg, Jesper Tegnér, Johan Björkegren. Carotid Plaque Age Is a Feature of Plaque Stability Inversely Related to Levels of Plasma Insulin. PLoS ONE, 2011; 6 (4): e18248 DOI: 10.1371/journal.pone.0018248