Impact of high-fat diet on red blood cells may cause cardiovascular disease

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University of Cincinnati (UC) researchers have discovered the negative impact a high fat diet has on red blood cells and how these cells, in turn, promote the development of cardiovascular disease.

This is one of the first studies to demonstrate the effect of red blood cells on the disease and could also affect the way patients with other health conditions, like cancer, who are prone to developing cardiovascular issues, are diagnosed and treated. It will be published in the Nov. 17 edition of the journal *Circulation* with an accompanying editorial.

"Obesity caused by chronic consumption of a high-calorie, high-fat diet is a worldwide epidemic, representing one of the greatest threats to global health," says principal investigator Vladimir Bogdanov, PhD, associate professor and director of the Hemostasis Research Program within the Division of Hematology Oncology at the UC College of Medicine and member of the Cincinnati Cancer Center and UC Cancer Institute. "White blood cells play a key role in fueling adipose tissue (fat) inflammation and insulin resistance in obesity and also promote the clogging of arteries, or atherosclerosis, setting the stage for heart attack and stroke. While these outcomes linked with a high fat diet and fat in the blood on white blood cells have been shown in animal models and humans, the impact of high fat diets on other bone marrow-derived cells, like red blood cells, is not well defined.

"Evidence is emerging that red blood cells play an important regulatory

role in the development of atherosclerosis, binding pro-inflammatory proteins that cause dysfunction in the inner lining of the blood vessel wall—the endothelium. We explored how a high fat-diet causes red blood cell dysfunction in this study."

Bogdanov and his team fed a 60 percent high-fat diet to a group of animal models for 12 weeks and saw an increased amount of key proteins that stimulate white blood cells bound to red blood cells. These white blood cells, also known as macrophages, are a type of white blood cell that "eats" cellular debris, foreign substances, microbes, cancer cells and anything else that does not have the types of proteins specific to the surface of healthy body cells on its surface. They also play a crucial role in atherosclerosis.

"In red blood cells from animal models fed a high-fat diet, there was an increase in cholesterol found in the cell membrane and phosphatidylserine levels, promoting inflammatory reactions. Phosphatidylserine is a phospholipid membrane component which plays a key role in the cycle of cells," Bogdanov says. "When red blood cells from the animals being fed the high-fat diet were injected into a control group, eating a normal diet, there was a three-fold increase in their spleens' uptake of red blood cells. The spleen is involved in the removal of blood cells, as well as systemic inflammation.

"All of these findings show that the dysfunction of red blood cells, corresponding with dysfunction of the lining of blood vessels, occurs very early in diet-induced obesity and may play a part in the formation of atherosclerosis. Diets high in saturated fat have long been associated with endothelial dysfunction, the precursor to atherosclerosis, but to our knowledge, the effects of high-fat diet on red blood cells have not been rigorously examined."

He adds that in humans, high cholesterol is associated with alterations in

red blood cells which are improved by treatment with statins, but the majority of obese humans do not have severe high cholesterol as was the case with the animal models in the study.

Bogdanov stresses that this project would have never been successful were it not for a close collaboration between his lab and that of Professor Neal Weintraub, MD, from the Vascular Biology Center at the Medical College of Georgia, Georgia Regents University (GRU). Weintraub, who is a co-principal investigator and a former UC faculty member, is working on expanding the team's findings in animal models to human disease. His team has recently conducted a study which demonstrated that a single high-fat meal produces harmful effects on red blood cells in humans. Bogdanov adds that these findings may also help patients with cancer who are frequently prone to thrombosis (blood clots).

This study was funded with start-up funds contractually given to Bogdanov upon his arrival at the university. Bogdanov cites no conflict of interest.

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