Red meat and cardiovascular diseases: the role of the microbiome

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A clinical study has shown that people who regularly eat red meats exhibit elevated blood levels of TMAO, a molecule produced by the intestinal bacteria, which is associated with an increase in the risk of cardiovascular events.

Aside from risk factors that are already well established for cardiovascular diseases (smoking, excess weight, diabetes, stress, sedentariness, poor diet), the work of Dr. Stanley Hazen's group (Cleveland Clinic) has shown that the intestinal bacteria (the microbiome) can itself also influence the formation of plaque in the artery walls.

These bacteria possess the ability to metabolize certain molecules (phosphatidylcholine, choline and carnitine) contained within foods of animal origin such as meat and eggs, into a metabolic waste product called trimethylamine (TMA). This TMA is processed by the liver where it is transformed into TMA N-oxide (TMAO), a highly inflammatory molecule which accelerates the development of atherosclerotic plaques and increases the reactivity of blood platelets (and thus the potential to form blood clots) in animal models[1].

A similar phenomenon seems to exist in humans because several observations indicate that elevated blood levels of TMAO are correlated with an increased risk of major cardiac events (sudden death, heart attack, stroke)[2]. Along the same lines, patients who are at very high risk of cardiovascular diseases due to a large quantity of atherosclerotic plaque in their blood vessels show blood levels of TMAO that are much higher than in patients who exhibit lower levels of atherosclerosis.

DIFFERENCES BETWEEN MEATS

The link between the production of TMAO and the consumption of red meats is well illustrated by the results of a clinical study recently published in the *European Heart Journal*[3].

In this study 113 volunteers were administered three isocaloric diets, each containing 25% protein derived from one of three different sources, i.e. red meats, white meats (poultry) or proteins of plant origins (beans, nuts, whole grains). Each participant spent four weeks following each of the diets, interspersed with "rest" periods of about one month during which they ate normally. During each of the periods in which the diets were followed, the researchers measured the amounts of TMAO present in the blood or excreted into the urine.

The researchers found that daily consumption of red meat, equivalent to a 225 g steak or two patties of ground beef, was associated with a significant increase (2 to 3 times) in the blood and urinary levels of TMAO, whereas consumption of white meat or plant-based proteins had no such effect. This increase is caused by an increase in the production by intestinal bacteria of TMA (and thus of TMAO) due to the carnitine present in the meat, as well as by a reduction in excretion of TMAO by the kidneys. It is interesting to note that this increase in TMAO is completely reversible and disappears rapidly after the consumption of red meat ceases.

These observations thus confirm that regular intake of red meat represents the principal dietary factor responsible for the formation of TMAO, which could explain the increased risk of cardiovascular diseases and of premature death observed in people who consume a lot of red meats and cured meats.

PREVENT THE PRODUCTION OF TMAO

Replacing red meats by poultry or by plant protein thus represents a simple way of reducing the production of TMAO by the microbiome and, at the same time, reducing the risk of cardiovascular diseases. It should also be noted that 3,3-dimethyl-1-butanol, another substance found naturally in certain foods such as red wine and olive oil, blocks the production of TMAO by different strains of bacteria and prevents the formation of atherosclerotic lesions in animal models[4]. Because these two foods are basic constituents of the Mediterranean diet, this blockage could participate in the protective effect against cardiovascular diseases that has been well documented for this style of eating.

(1) Koeth RA et al. Intestinal microbiota metabolism of L-carnitine, a nutrient in red meat, promotes atherosclerosis. Nature Med. 2013; 19: 576-585.
(2) Tang WH et al. Intestinal microbial metabolism of phosphatidylcholine and cardiovascular risk. N. Engl. J. Med. 2013; 368: 1575-1584.
(3) Wang Z et al. Impact of chronic dietary red meat, white meat, or non-meat protein on trimethylamine N-oxide metabolism and renal excretion in healthy men and women. Eur. Heart J., published online December 10 2018.
(4) Wang Z et al. Non-lethal inhibition of gut microbial trimethylamine production for the treatment of atherosclerosis. Cell 2015; 163: 1585-1595.

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