

# Taking a Closer Look at TMAO

## What is TMAO?

TMAO (or trimethylamine N-oxide) is a metabolite produced by gut bacteria. Briefly, nutrients such as phosphatidylcholine (also known as lecithin), choline, and L-carnitine are abundant in animal-derived products such as red meat, egg yolk and full-fat dairy products. When consumed, these nutrients are processed by gut bacteria resulting in the release of various metabolites including TMA (trimethylamine) into the blood. TMA is then transported to the liver where it is converted into TMAO which has been shown to regulate various physiological processes involved in the development of atherosclerosis<sup>1,2</sup>.

## What foods are rich in dietary TMAO precursors?

Red Meat	Full-Fat Dairy Products	Others
Beef Pork Ham Lamb Veal Processed meats	Whole milk Eggs Yogurt Cream cheese Butter	Energy drinks Dietary supplements

## What dietary modification may help reduce an elevated TMAO?

The composition of the diet can have a dramatic effect on the composition of the gut microbiome. Through dietary modifications, including the elimination of TMAO precursors, the gut bacteria may be altered and TMAO levels reduced. Foods commonly found in the Mediterranean diet such as cold-pressed olive oil, balsamic vinegar, and red wine are rich in the compound DMB (or 3,3-dimethyl-1-butanol), which has been shown to inhibit TMAO production<sup>3</sup>.

## My patient is taking a fish oil/krill oil supplement, will it falsely elevate their TMAO results?

To date, we know that TMAO is found in high levels in certain types of seafood. A comprehensive list of the contents in supplements are rarely listed, so it is possible that TMAO may be present in fish oil/krill oil supplements. To avoid potential false elevations in TMAO results, we recommend the patient abstain from eating fish and taking a fish oil/krill oil supplement 24 hours prior to their blood draw for the TMAO test.

## If a patient has an elevated TMAO and they modify their diet, how long should the physician wait to repeat the test?

To date, there is no evidence published demonstrating how long it takes to lower baseline TMAO levels. Dramatically changing the gut microbiome through diet alone may take weeks to months. Therefore, a meaningful shift in the gut community affecting TMAO production may take weeks to months as well. We are currently suggesting a 3 to 6 month follow-up time, but this may change as we gather more information.

## If a patient begins taking pre/probiotics, how long until they change their gut bacteria?

Similar to dietary modifications, pre/probiotics may take weeks to months to make a meaningful shift in the gut bacteria community. Pre/probiotics have been proven to help maintain a diverse 'healthy' gut<sup>4</sup>, but have not been scientifically shown to reduce TMAO levels.

## Is TMAO a marker for Small Intestinal Bacterial Overgrowth (SIBO)?

To date, the literature has not demonstrated a link between TMAO and SIBO. There are many types of disorders that fall under the umbrella of gut dysfunction. SIBO is a type of gut dysfunction and is primarily attributable to GI nerve dysregulation. Excess TMAO production is a type of gut dysfunction indicating the intestine (primarily large intestine) has excess bacteria capable of producing TMAO. The TMAO test does not indicate the location of TMAO producing bacteria in the gut, only the presence.

## Animal-Derived Foods

- Red Meat
- Full-Fat Dairy Products
- Egg Yolk

## Dietary Nutrients

- L-Carnitine
- Phosphatidylcholine
- Choline

Conversion of  
nutrients to TMA by  
gut microbiome

GUT FLORA

Trimethylamine  
(TMA)

Conversion to  
TMAO by liver  
enzymes

LIVER

Trimethylamine-*N*-oxide  
(TMAO)

Atherosclerosis

Stroke

Heart attack

Death

## References

1. Wang Z et al. Gut flora metabolism of phosphatidylcholine promotes cardiovascular disease. *Nature*. 2011; 472: 57–63. 2. Koeth RA et al. Intestinal microbiota metabolism of L-carnitine, a nutrient in red meat, promotes atherosclerosis. *Nat Med*. 2013; 19: 576–585. 3. Wang Z et al. Non-lethal Inhibition of Gut Microbial Trimethylamine Production for the Treatment of Atherosclerosis. *Cell*. 2015; 163: 1585–1595. 4. Bäckhed F et al. Defining a healthy human gut microbiome: current concepts, future directions, and clinical applications. *Cell host & microbe* 2012; 5: 611–622.



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