

TRIMETHYLAMINURIA

By Professor Elizabeth Shephard for MEBO Research

Index of documentation	Page number
1. Trimethylaminuria	2
2. Scientific basis	2
3. Diagnosis and Management	3
4. Internet links on Trimethylaminuria	3
5. Letter from Maria de la Torre	4
6. Letter from Dr Cheryl Fields	9
7. Letter from Karen James	12

1. Trimethylaminuria

Trimethylaminuria (TMAU) is a condition in which sufferers have an extremely unpleasant body odor. They excrete the chemical trimethylamine (TMA) in their breath, sweat and urine. TMA is the chemical to which the human nose is most sensitive and is the same chemical that gives rotting fish its unpleasant smell. This is the reason why, for many years, the condition was referred to as fish-odor syndrome.

An affected person has to cope with the unpleasant symptoms of their condition, caused by high amounts of TMA circulating in their body and in their bodily secretions, and the prejudices of society to those that have a body odor. TMAU individuals therefore experience medical, psychological and social problems, which impact not only on their lives, but also on the lives of their families. Suicidal feelings, social isolation, broken relationships, depression, lack of understanding by work colleagues, all contribute to the difficulties faced by those that must live with the devastating consequences of TMAU. A few cases of TMAU with associated epileptic-like fits have been reported. Some TMAU patients exhibit episodic body odor and their bad experiences are compounded if the medical practitioner consulted, perceives the condition to be imaginary.

A shower is not the solution for TMAU. This is not a hygiene problem.

TMAU is reported in all ethnic groups and in both genders. Symptoms are usually present from birth and may worsen during puberty. In females, because of hormonal changes, symptoms are more severe just before and during menstruation, after taking oral contraceptives, and around the time of menopause.

2. Scientific basis for Trimethylaminuria

TMAU has been identified as an inherited, recessive disorder caused by mutations in the flavin-containing monooxygenase 3 gene, *FMO3*. The protein FMO3 changes the odorous TMA to the chemical TMA *N*-oxide, which does not smell. Depending on the severity of the mutation, this conversion process is absent, or severely impaired, in those with TMAU.

The chemical TMA is produced from normal dietary components such as choline, found in many foods e.g. milk, red meat, eggs and soya. In the gut, bacteria convert choline

into betaine. TMA is then produced from betaine by a bacterial enzyme. The TMA produced in the gut is then rapidly absorbed and, in the liver, the enzyme FMO3 converts the TMA to TMA *N*-oxide. See Figure 1.

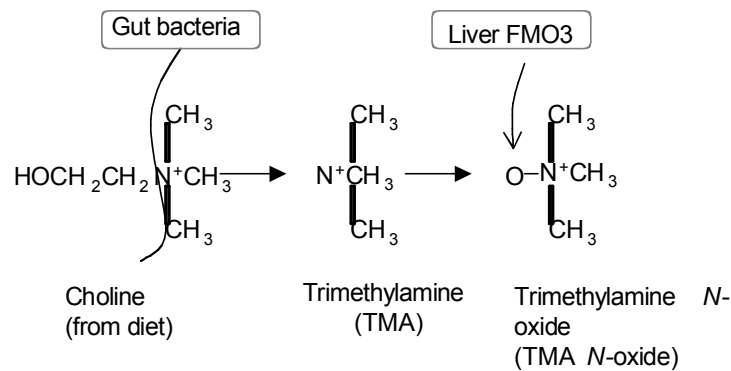


Figure 1. Simplified pathway showing production of TMA in the gut, and its conversion to TMA *N*-oxide in the liver by the action of the protein FMO3. The action of FMO3 is absent or impaired in Trimethylaminuria.

3. Diagnosis and management

TMAU is diagnosed by an increased ratio in the urine of TMA:TMA *N*-oxide [1.2]. Subsequent genetic analysis of the *FMO3* gene can be used to identify specific mutations that cause the disorder [1.2].

Management of TMAU is not satisfactory. Courses with antibiotics, to kill gut bacteria, may work temporarily for some patients to alleviate the symptoms. However, such treatments are not sustainable and do not work for most with TMAU. Strict dietary control, that eliminates foodstuffs that lead to TMA production, is recommended. However, maintaining a diet low in choline is both difficult and unhealthy, and in itself can lead to further medical problems.

4. Internet links for Trimethylaminuria

<http://www.ncbi.nlm.nih.gov/books/NBK1103/>

[1] Phillips IR Shephard EA, (2007 and updated 2011) Trimethylaminuria. In: GeneReviews at GeneTests: Medical Genetics Information Resource .Copyright, University of Washington, Seattle.

<http://www.eurogentest.org/web/info/public/unit3/geneCards.xhtml>

then click in the index on 'Trimethylaminuria' to access the article:

[2] Shephard EA, Treacy EP, Phillips IR (2012). Clinical utility gene card for: Trimethylaminuria.. Eur J Hum Genet, advanced online publication (doi:10.1038/ejhg.2011.214).

<http://www.youtube.com/user/TheCalmwaves/videos>

A collection of video clips on TMAU