

Title: Primary Trimethylaminuria *GeneReview* – Suggestive Findings  
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### Specific Methods of Detecting TMA and TMA N-Oxide in Urine

The methods of detecting TMA and TMA *N*-oxide in urine currently available involve sophisticated equipment and require skilled and experienced personnel:

- **Head-space gas chromatography (GC) or GC-mass spectrometry** [Mills et al 1999]. Disadvantages: GC techniques are time consuming, TMA *N*-oxide must be chemically reduced to TMA before analysis, and both TMA and TMA produced by reduction of TMA *N*-oxide must be extracted from urine.
- **Mass spectrometry (MS)**<sup>\*</sup> including fast atom bombardment MS (FAB-MS) [Mamer et al 1999], electrospray ionization tandem MS (ESI-MS/MS) [Johnson 2008], direct infusion electrospray quadrupole time-of-flight MS [Mamer et al 2010], or matrix-assisted laser desorption/ionization time-of-flight MS (MALDI-TOFMS) [Hsu et al 2007]
- **Proton nuclear magnetic resonance (NMR) spectroscopy**<sup>\*</sup> [Maschke et al 1997, Murphy et al 2000, Podadera et al 2005, Lee et al 2006]

<sup>\*</sup> **MS** and **proton NMR** have the advantage of being able to detect TMA and TMA *N*-oxide simultaneously with great sensitivity. NMR has the further advantage of requiring no prior extraction or separation of metabolites and thus measurement can be done directly on urine samples.

### References

Hsu WY, Lo WY, Lai CC, Tsai FJ, Tsai CH, Tsai Y, Lin WD, Chao MC. Rapid screening assay of trimethylaminuria in urine with matrix-assisted laser desorption/ionization time-of-flight mass spectrometry. *Rapid Commun Mass Spectrom* 2007;21:1915-9.

Johnson DW. A flow injection electrospray ionization tandem mass spectrometric method for the simultaneous measurement of trimethylamine and trimethylamine *N*-oxide in urine. *J Mass Spectrom* 2008;43:495-9.

Lee MB, Storer MK, Blunt JW, Lever M. Validation of (1)H NMR spectroscopy as an analytical tool for methylamine metabolites in urine. *Clin Chim Acta* 2006;365:264-9.

Mamer OA, Choiniere L, Lesimple A. Measurement of urinary trimethylamine and trimethylamine oxide by direct infusion electrospray quadrupole time-of-flight spectrometry. *Anal Biochem* 2010;406:80-2.

Mamer OA, Choiniere L, Treacy EP. Measurement of trimethylamine and trimethylamine *N*-oxide independently in urine by fast atom bombardment mass spectrometry. *Anal Biochem* 1999;276:144-9.

Maschke S, Wahl A, Azaroual N, Boulet O, Crunelle V, Imbenotte M, Foulard M, Vermeersch G, Lhermitte M. 1H-NMR analysis of trimethylamine in urine for the diagnosis of fish-odour syndrome. *Clin Chim Acta* 1997;263:139-46.

Mills GA, Walker V, Mughal H. Quantitative determination of trimethylamine in urine by solid-phase microextraction and gas chromatography-mass spectrometry. *J Chromatogr B Biomed Sci Appl* 1999;723:281-5.

Murphy HC, Dolphin CT, Janmohamed A, Holmes HC, Michelakakis H, Shephard EA, Chalmers RA, Phillips IR, Iles RA. A novel mutation in the flavin-containing monooxygenase 3 gene, FM03, that causes fish-odour syndrome: activity of the mutant enzyme assessed by proton NMR spectroscopy. *Pharmacogenetics* 2000;10:439-51.

Podadera P, Areas JAG, Lanfer-Marquez UM. Diagnosis of suspected trimethylaminuria by NMR spectroscopy. *Clin Chim Acta* 2005;351:149-54.