National Health and Nutrition Examination Survey 2003-2004

Documentation, Codebook, and Frequencies

Laboratory Component:
Methylmalonic acid and Homocysteine

Survey Years:
2003 to 2004

SAS Export File:
L06MH_C.XPT

First Published: June 2006
Last Revised: July 2007

NHANES 2003–2004 Data Documentation

Laboratory Assessment: Lab 06mh–Methylmalonic acid and Homocysteine

Years of Coverage: 2003–2004 **First Published:** June 2006 **Last Revised:** July 2007

This is being updated to add methylmalonic acid and a homocsteine analytical note.

Component Description

Methylmalonic acid and Homocysteine

The objectives of this component are: 1) to provide data for monitoring secular trends in measures of nutritional status in the U.S. population; 2) to evaluate the effect of people's habits and behaviors such as physical activity and the use of alcohol, tobacco, and dietary supplements on people's nutritional status; and 3) to evaluate the effect of changes in nutrition and public health policies including welfare reform legislation, food fortification policy, and child nutrition programs on the nutritional status of the U.S. population. These data will be used to estimate deficiencies and toxicities of specific nutrients in the population and subgroups, to provide population reference data, and to estimate the contribution of diet, supplements, and other factors to serum levels of nutrients. Data will be used for research to further define nutrient requirements as well as optimal levels for disease prevention and health promotion.

Eligible Sample

Methylmalonic acid and Homocysteine

Participants aged 3 year and older who do not meet any of the exclusion criteria are eligible.

Description of Laboratory Methodology

Methylmalonic acid

Methylmalonic acid (MMA) is extracted from plasma along with an added internal standard using an anion exchange resin (1). The extracted acid is then derivatized with cyclohexanol to form a dicyclohexyl ester. The derivatized samples are injected onto a gas chromatograph for separation from other constituents. The effluent from the gas chromatograph is monitored with a mass selective detector using selected ion monitoring. Results are quantitated by internal calibration using peak area ratios of MMA and the internal standard (d3MMA).

Increased concentrations of methylmalonic acid in plasma or serum and excessive urinary excretion of MMA are believed to be direct measures of tissue stores of cobalamin (vitamin B12) and to be the first indication of cobalamin deficiency (2). The concentration of MMA in plasma or serum was found to be a useful indicator of cobalamin deficiency, especially in patients with few or no hematological abnormalities, normal results for the Schilling test, or normal or only slightly depressed serum cobalamin concentrations (3). In folate deficiency, methylmalonic acid is normal. Methylmalonic acid may be elevated due to inborn errors of metabolism.

The range of methylmalonic acid in plasma from "healthy adults" is 0.05 to 0.26 umol/L (4).

An international round robin performed in 1999 (5) demonstrated that this method is fully equivalent to the original method of Rasmussen (1), but also to the method of Marcell et al. (6).

Homocysteine

The method is a fluorescence polarization immunoassay (FPIA) from Abbott Diagnostics. Total homocysteine (tHcy) in plasma is measured by the Abbott Homocysteine assay on the Abbott AxSym analyzer, a fully automated FPIA method. DTT reduces homocysteine bound to albumin and to other small molecules, homocysteine, and mixed disulfides, to free thiol. S-adenosylhomocysteine (SAH) hydrolase catalyzes conversion of homocysteine to SAH in the presence of added adenosine. The specific monoclonal antibody and the fluoresceinated SAH analog tracer constitute the FPIA detection system. Plasma total homocysteine concentrations are calculated by the Abbott AxSym Immunoassay Analyzer using a machine-stored calibration curve.

As part of ongoing methods comparisons studies, an international round robin was conducted in 1998. Results obtained using the FPIA method described earlier were compared to results obtained using high performance liquid chromatography (HPLC) with fluorometric detection at 385 nm excitation and 515 nm emission. The international round robin demonstrated that the FPIA method was fully equivalent to other frequently used methods (i.e., HPLC-FD, HPLC-ED, and GC/MS). Thus, the Abbott Homocysteine assay was used as the primary method for determination of plasma total homocysteine in NHANES 2003–2004.

Laboratory Quality Control and Monitoring

The NHANES quality control and quality assurance protocols (QA/QC) meet the 1988 Clinical Laboratory Improvement Act mandates. Detailed quality control and quality assurance instructions are discussed in the NHANES Laboratory/Medical Technologists Procedures Manual (LPM). Read the LABDOC file for detailed QA/QC protocols.

Data Processing and Editing

Plasma specimens are processed, stored, and shipped to the Division of Environmental Health Laboratory Sciences, National Center for Environmental Health, Centers for Disease Control and Prevention for analysis.

Detailed specimen collection and processing instructions are discussed in the NHANES Laboratory/Medical Technologists Procedures Manual (LPM). Vials are stored under appropriate frozen (–20°C) conditions until they are shipped to National Center for Environmental Health for testing.

This file contains no top coding.

Analytic Notes

The analysis of NHANES 2003–2004 laboratory data must be conducted with the key survey design and basic demographic variables.

The NHANES 2003–2004 Household Questionnaire Data Files contain demographic data, health indicators, and other related information collected during household interviews. The Household Questionnaire Data Files also contain all survey design variables and sample weights required to analyze these data. The Phlebotomy Examination file includes auxiliary information on duration of fasting, the time of day of the venipuncture, and the conditions precluding venipuncture. The Household Questionnaire and Phlebotomy Exam files may be linked to the laboratory data file using the unique survey participant identifier SEQN.

Homocysteine method change:

The Homocsteine (uMol/L) method changed in 2002 from an Abbott IMX to an Abbott AxSym method. A crossover study was performed and revealed the following Deming regression (n=361, r**2 = 0.9817):

AxSym = 10**(0.983*log10(IMX) + 0.0418)

References

1. Rasmussen K. Solid-phase sample extraction for rapid determination of methylmalonic acid in serum and urine by a stable-isotope-dilution method. Clin Chem 1989;35(2):260-4.

2. Moelby L, Rasmussen K, Jensen MK and Pedersen KO. The relationship between clinically confirmed cobalamin deficiency and serum methylmalonic acid. J Intern Med 1990;228:373-78.

3. Rasmussen K, Moller J, Lyngbak M, Holm Pedersen A-M, Dybkjaer L. Age- and gender-specific reference intervals for total homocysteine and methylmalonic acid in plasma before and after vitamin supplementation. Clin Chem 1996;42(4):630-6.

4. Holleland G, Schneede J, Ueland PM, Lund PK, Refsum H, Sandberg S. Cobalamin deficiency in general practice. Assessment of the diagnostic utility and cost benefit analysis of methlymalonic acid determination in relation to current diagnostic strategies. Clin Chem 1999;45(2):189-98.

5. Pfeiffer CM, Smith SJ, Miller DT, Gunter EW. Comparison of serum and plasma methylmalonic acid measurements in 13 laboratories: an international study. Clin Chem 1999;45(12):2236-42.

6. Marcell PD, Stabler SP, Podell ER, Allen RH. Quantitation of methylmalonic acid and other dicarboxylic acids in normal serum and urine using capillary gas chromatography-mass spectrometry. Anal Biochem 1985;150:58-66.

Locator Fields

Title: Methylmalonic acid and Homocysteine
Contact Number: 1-866-441-NCHS

Years of Content: 2003–2004

First Published: June 2006

Revised: July 2007

Access Constraints: None

Use Constraints: None

Geographic Coverage: National

Subject: Methylmalonic acid and Homocysteine
Record Source: NHANES 2003–2004

Survey Methodology: NHANES 2003–2004 is a stratified multistage probability sample of the civilian non-institutionalized population of the U.S.

Medium: NHANES Web site; SAS transport files

National Health and Nutrition Examination Survey
Codebook for Data Production (2003-2004)

Methylmalonic acid and Homocysteine (L06MH_C)
Person Level Data

First Published: June 2006
Last Revised: July 2007

SEQN	Target
	B(3 Yrs. to 150 Yrs.)
Hard Edits	**SAS Label**
	Respondent sequence number
English Text: Respondent sequence number.	
English Instructions:	

LBXHCY	Target
	B(3 Yrs. to 150 Yrs.)
Hard Edits	**SAS Label**
	Homocysteine (umol/L)
English Text: Homocysteine(umol/L)	
English Instructions:	

Code or Value	Description	Count	Cumulative	Skip to Item
1.79 to 116.21	Range of Values	7888	7888	
.	Missing	668	8556	

LBXMMA	Target
	B(3 Yrs. to 150 Yrs.)
Hard Edits	**SAS Label**
	Methylmalonic acid (umol/L)
English Text: Methylmalonic acid (umol/L)	
English Instructions:	

Code or Value	Description	Count	Cumulative	Skip to Item
0.048 to 10.558	Range of Values	7501	7501	
0.035	Below Limit of Detection	43	7544	
.	Missing	1012	8556	