Vitamin E (plasma, serum)

1 Name and description of analyte

1.1 Name of analyte
Vitamin E

1.2 Alternative names
Vitamin E refers to a group of tocopherols and tocotrienols. Alpha tocopherol is the most abundant and biologically active form.

1.3 NLMC code (authors please leave this field blank)

1.4. Function(s) of analyte
Vitamin E is a fat soluble antioxidant, acting as a scavenger for free radicals. The most well defined role of vitamin E is protection of lipids from oxidation, particularly in cell membranes. In addition, the antioxidant properties of vitamin E have been linked with prevention of retinopathy in preterm infants, as well as protection of red blood cells from haemolysis, inhibition of inflammation, and have been identified as necessary for neurologic and reproductive functions.

2 Sample requirements and precautions

2.1 Medium in which measured
Vitamin E is usually measured in serum or plasma.

2.2 Precautions re sampling, handling etc.
Samples should be protected from light and stored frozen.

3 Summary of clinical uses and limitations of measurements

3.1 Uses
Detection of vitamin E deficiency and monitoring of response to treatment, including patients who are receiving nutritional support.

3.2 Limitations
Vitamin E circulates in the blood bound to low density β-lipoproteins and pre-albumin. If serum lipid concentrations increase, vitamin E partitions out of the cell membrane with the circulating lipoproteins. A higher vitamin E level may then be observed with elevated serum lipids, masking vitamin E deficiency. Vitamin E status may be determined by expressing the vitamin E concentration as a ratio to the lipid (usually cholesterol) concentration.

4 Analytical considerations

4.1 Analytical methods
Vitamin E can be measured directly using the following methods:
1) HPLC with fluorescence, electrochemical or UV detection
2) gas chromatography–isotope dilution Mass spectrometry (GC-IDMS)
3) photometric or fluorimetric measurement based on the Emmerie-Engel procedure (tocopherol oxidised to tocopheryl quinine by $FeCl_3$

with the resultant Fe^{2+} coupled with α,α'-dipyridyl to form a red colour).

4) thin layer and gas chromatography, which can be used to separate the tocopherols and tocotrienols.

Functional methods include:

1) erythrocyte haemolysis test: haemolysis produced during incubation of erythrocytes with hydrogen peroxide or dialuric acid is proportional to plasma concentration of vitamin E.
2) malondialdehyde test: malondialdehyde produced is measured following incubation of erythrocytes with hydrogen peroxide.

4.2 Reference method

Gas chromatography–isotope dilution–mass spectrometry (GC–IDMS)

4.3 Reference materials

Alpha tocopherol (Standard Reference Material (SRM) 968e**,** National Institute of Standards and Technology (NIST), United States). Assigned value: 15.2–45.0 µmol/L.

Gamma tocopherol (SRM 968e**,** National Institute of Standards and Technology (NIST), United States). Assigned value: 3.44–5.45 µmol/L.

4.4 Interfering substances

No interfering substances identified for HPLC analysis of vitamin E.

4.5 Sources of error

Vitamin E concetrations can decrease if samples are not protected from light.

5 Reference intervals and variance

5.1.1 Reference interval (adults)

Serum or heparinised plasma:
12-42 µmol/L
(from: Burtis C A, Ashwood E R, Bruns D E. (Eds) Tietz Textbook of Clinical Chemistry and Molecular Diagnostics (5th edn). St Louis, USA: Elsevier,2012.

5.1.2 Reference intervals (others)

Serum or heparinised plasma:
Premature neonates: 2.3-11.6 µmol/L
Children (1-12 years): 7-21 µmol/L
Adolescents (13-19 years): 14-23 µmol/L
(from: Burtis C. A, Ashwood, E. R., and Bruns, D. E. Tietz Textbook of Clinical Chemistry and Molecular Diagnostics. Fifth edition (2012))

5.1.3 Extent of variation

5.1.3.1 Interindividual CV 39.8%[1] / 19.9%[2]

5.1.3.2 Intraindividual CV 13.9%[1] / 15.2%[2]

5.1.3.3 Index of individuality 0.35[1]

[1]Lacher D A, Hughes J P, Carroll M D. Biological Variation of Laboratory Analytes Based on the 1999-2002 National Health and Nutrition

Examination Survey. National Health Statistics Reports No. 21, March 2010.

[2] Sebastian-Gambaro, M. A., Liron-Hernandez, F. J., and Fuentes-Arderiu, X. Intra- and Inter-Individual Biological Variability Data Bank. Eur J Clin Chem Clin Biochem (1997) 35:845-852.

5.1.3.4 CV of method <5%

5.1.3.5 Critical difference 43%

5.1.4 Sources of variation

Vitamin E circulates in blood bound to low density β-lipoproteins, therefore changes in lipid concentration will affect vitamin E concentrations. Seasonal variation in vitamin E levels have been described in some studies with lower levels reported in the spring, and peak levels observed in the autumn.

6 Clinical uses of measurement and interpretation of results

6.1 Indications and interpretation

Monitoring of patients who are susceptible to vitamin E deficiency including patients with cystic fibrosis, pancreatic insufficiency, and liver disease. monitoring of patients who are receiving nutritional support.

6.2 Confounding factors

Vitamin E is lipid soluble and is bound to lipoproteins in the circulation. Elevated lipid concentrations can result in increased circulating vitamin E levels, and can therefore mask vitamin E deficiency.

7 Causes of abnormal results

7.1 High values

7.1.1 Causes

Excess vitamin E intake is usually only achieved by dietary supplementation. Vitamin E has low toxicity and the effects of excess vitamin E are linked with predisposition to bleeding through interference with the absorption of vitamin K.

7.1.2 Investigation

Not usually required.

7.2 Low values

7.2.1 Causes

Vitamin E deficiency may occur in preterm and low birth weight infants due to their limited adipose tissue and the poor transfer of vitamin E across the placenta. Signs of deficiency include irritability, haemolytic anaemia, thrombocytopenia, and oedema. Vitamin E deficiency is rare in children and adults, but may occur in fat malabsorption states such as cystic fibrosis, and chronic cholestasis or in genetic abnormalities of lipoprotein metabolism such as abetailipoproteinemia where patients lack the apolipoprotein B required to transfer vitamin E from enterocytes to plasma.

7.2.2 Investigation
Investigation of vitamin E deficiency may be a challenge as serum vitamin E levels depend on serum lipid levels and may not reflect tissue levels.

7.3 Notes
None.

8 Performance

8.1 Sensitivity, specificity etc. for individual conditions
Not applicable.

9 Systematic reviews and guidelines

9.1 Systematic reviews
Several reviews on the association of vitamin E with diseases and disease prevention are available including:
Brion L P, Bell E F, Raghuveer T S. Vitamin E supplementation for prevention of morbidity and mortality in preterm infants. Cochrane Database Syst Rev 2003; CD003665.

9.2 Guidelines
Cystic Fibrosis Trust: Standards for the Clinical Care of Children and Adults with Cystic Fibrosis in the UK (2nd edn). 2011.
http://www.cysticfibrosis.org.uk/media/448939/cd-standards-of-care-dec-2011.pdf

9.3 Recommendations
None Identified.

10 Links

10.1 Related analytes
Cholesterol for assessment of lipid status.

10.2 Related tests
Vitamin E is often measured simultaneously with vitamin A.

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