

Vitamin A (plasma, serum)

1 Name and description of analyte

1.1 Name of analyte
Vitamin A

1.2 Alternative names
Vitamin A refers to a group of compounds including retinol, retinal, retinoic acid, and several vitamin A precursors such as β -carotene. Retinol is the principal circulating form of vitamin A.

1.3 NLMC code (to follow)

1.4. Functions of analyte

- 1) The most important role of vitamin A is in vision and generation of photosensitive products. 11-cis-retinal is found in opsin products in rods (rhodopsin) and cones (iodopsins). Light causes cis-retinal to convert to the trans isomer and is released from the opsin. This triggers changes in membrane potentials and optic nerve transmission.
- 2) Retinol and retinoic acid are involved in the control, differentiation and proliferation of epithelial cells and other cells such as bone, and have a role in mucin secretion and bone growth.
- 3) Retinyl phosphate is a carrier of mannose and has a role in the synthesis of mannose containing glycoproteins.
- 4) Vitamin A has a role in reproduction, growth, embryonic development and immune function, mediated through binding of retinoic acid to nuclear receptors regulating gene expression.

2 Sample requirements and precautions

2.1 Medium in which measured
Vitamin A is measured in serum or plasma.

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

3 Summary of clinical uses and limitations of measurements

3.1 Uses
Detection of vitamin A deficiency and toxicity as well as monitoring response to treatment including patients on nutritional support.

3.2 Limitations
Vitamin A is stored in the liver and mobilisation into plasma is affected by the availability of binding proteins. Measurement of serum vitamin A may not be a true reflection of total body concentration; serum concentrations may not decline until liver stores have been critically depleted, and low serum vitamin A concentrations may be observed due to decreased concentrations of binding proteins even when hepatic stores are adequate.

4 Analytical considerations

4.1 Analytical methods

- 1) HPLC is the most commonly used method. Both normal and reverse phase chromatography may be used. With normal phase, compounds to be separated are adsorbed onto microparticulate silica gel and eluted in order of most polar to least polar. Photometric, electrochemical and mass spectrophotometric detectors may be used to detect vitamin A following chromatography.
- 2) Other methods for measurement of vitamin A include:
 - tandem mass spectrometry
 - gas chromatography–isotope dilution mass spectrometry (GC-IDMS)
 - Carr-price photometric method using antimony trichloride in chloroform
 - Neeld-Pearson method using trifluoroacetic acid to produce a blue pigment with the conjugated double bonds of vitamin A
 - Fluorometric or spectrophotometric measurement following solvent
- 3) Retinol binding protein and transthyretin may also be measured in order to assess vitamin A status as they complex with retinol in a 1:1:1 ratio. Retinol binding protein can be measured by radial immunodiffusion or nephelometry.

4.2 Reference method

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

4.3 Reference materials

Total retinol (Standard Reference Material (SRM) 968e, National Institute of Standards and Technology (NIST), United States). Assigned value: 1.19-2.26 $\mu\text{mol/L}$

4.4 Interfering substances

No interfering substances have been identified for HPLC analysis of vitamin A.

4.5 Sources of error

Concentrations of Vitamin A can decrease if samples are not protected from light.

5 Reference intervals and variance

5.1.1 Reference interval (adults)

1.05-2.80 $\mu\text{mol/L}$

(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)

1 to 6 year old children: 0.70-1.40 $\mu\text{mol/L}$

7 to 12 year old children: 0.91-1.71 $\mu\text{mol/L}$

13 to 19 year old adolescents: 0.91-2.51 $\mu\text{mol/L}$

(from: Burtis C A, Ashwood E R, Bruns DE. *ibid.*)

5.1.3 Extent of variation

5.1.3.1 Interindividual CV 31%¹

5.1.3.2 Intraindividual CV 10.4%¹/ 20.5%²

5.1.3.3 Index of individuality 0.33¹

5.1.3.4 Index of individuality 0.33¹

¹Lacher D A, Hughes J P, Carroll M D. Biological Variation of Laboratory Analytes. Based on the 1999-2002 National Health and Nutrition Examination Survey. Natl Health Stat Report 2010 Mar 1;(21):1-7.

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

5.1.3.5 CV of method <5%

5.1.3.6 Critical difference between 32% and 58%

5.1.4 Sources of variation

Vitamin A concentrations in men are generally 20% higher than in women.

6 Clinical uses of measurement and interpretation of results

6.1 Indications and interpretation

1. Monitoring of patients who are susceptible to vitamin A deficiency, e.g. patients with cystic fibrosis, pancreatic insufficiency, or liver disease.
2. Monitoring of patients who are receiving nutritional support.

6.2 Confounding factors

Measurement of serum/plasma vitamin A concentrations does not provide ideal assessment of vitamin A status as they may not decline until liver stores have been critically depleted.

Low serum vitamin A concentrations may be observed even with adequate hepatic stores owing to decreased availability of binding proteins. Retinol binding protein and transthyretin are negative acute phase proteins, therefore patients with systematic inflammatory response syndrome may have transient falls in both the binding proteins and retinol. Measurement of CRP may help to identify whether low vitamin A concentrations are due to inflammatory or nutritional causes.

7 Causes of abnormal results

7.1 High values

7.1.1 Causes

Vitamin A toxicity may occur due to excessive ingestion of vitamin A or inappropriate supplementation.

7.1.2 Investigation

Acute toxicity may present with symptoms of abdominal pain, nausea, vomiting, severe headaches, irritability and dizziness, while signs of chronic toxicity due to exposure of high concentrations of vitamin A over a prolonged period include bone and joint pain, hair loss, anorexia, benign intracranial hypertension and hepatomegaly

7.2 Low values

7.2.1 Causes

Vitamin A deficiency is more common in infants and children than in adults. It may be observed in premature infants because hepatic accumulation of vitamin A usually occurs within the last trimester of pregnancy. Vitamin A deficiency is also seen in individuals with fat malabsorption, such as caused by coeliac disease, chronic pancreatitis or cystic fibrosis, and protein-energy malnutrition. Liver damage may lead to reduced retinol binding protein synthesis.

7.2.2 Investigation

Vitamin A deficiency may be diagnosed clinically with confirmation of response to treatment (particularly in the developing world), or by the measurement of serum or plasma vitamin A concentrations. Clinical features of vitamin A deficiency include degenerative changes in the eyes, such as nyctalopia and xerophthalmia, where the conjunctiva becomes dry with small grey plaques with foamy surfaces (Bitot's spots), keratomalacia and blindness. Skin changes can include dryness, roughness, papular eruptions, and follicular hyperkeratosis.

7.3 Notes

Excess intake of vitamin A during the early stages of pregnancy has been shown to be teratogenic causing abnormalities derived from neural crest cells.

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 role of vitamin A in different diseases are available but no reviews relating to biochemical analysis of vitamin A have been identified.

9.2 Guidelines

Cystic Fibrosis Trust: Standards for the Clinical Care of Children and Adults with Cystic Fibrosis in the UK. Second Edition, December 2011.
<http://www.cysticfibrosis.org.uk/media/448939/cd-standards-of-care-dec-2011.pdf>

Recommends annual assessment of fat soluble vitamin concentrations.

9.3 Recommendations

None identified.

10 Links

10.1 Related analytes

None.

10.2 Related tests

Vitamin A is often measured simultaneously with vitamin E.

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