VITAMIN A (Retinol)

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Introduction

Vitamin A is essential throughout life as it is required in reproduction, embryonic and foetal development, vision, growth, differentiation and tissue maintenance [1]. The term vitamin A covers the retinoids, a group of lipid-soluble compounds which have similar physiological functions and metabolic activities: retinol, retinal (the aldehyde form), and retinoic acid. Retinol inter-converts between retinyl esters and retinal, while retinoic acid (which is not found in the diet) is an end product of retinol conversion. These substances have different actions: retinoic acid is required for the growth and differentiation of epithelial cells, whereas retinyl ester, retinol and retinal can all support cellular differentiation, reproduction and visual functions. Retinoic acid is the form of vitamin A for which a teratogenic effect on the foetus has been demonstrated and which acts as a hormone in many cells by regulating gene expression, thus controlling cell differentiation and maturation [2].

Vitamin A nutrition is quite complex and needs to be considered in terms of its relationship with other vitamins. For example, vitamin A works cooperatively at the genetic level with vitamin D. Vitamin E is required for the conversion of β-carotene to retinol (see below), while vitamin A absorption can be reduced by excess vitamin E consumption. In turn, excess dietary vitamin A can interfere with vitamin K absorption. The conclusion is that although supplementation with vitamin A may be appropriate in cases of proven deficiency, a vitamin-rich mixed diet is the best way to maintain optimum vitamin A status.

Food sources of vitamin A

Vitamin A can be obtained directly from animal products in the diet, such as liver or fortified milk. The vitamin can also be derived from the carotenoids, which are photosynthetic accessory pigments found in plant chloroplasts. Around 50 of the over 700 carotenoids occurring in nature can be converted to vitamin A by the action of an oxygenase enzyme present in the intestine and other tissues [3]. The major pro-vitamin A carotenoid in the human diet is β-carotene, although α-carotene and β-cryptoxanthin can make a small contribution. For nutritional purposes, the term "retinol equivalent" (RE) is used to convert all dietary sources of vitamin A and carotenoids in the diet into a single unit. 1 RE = 1 μg or 3.33 i.u. of retinol. 1.0 μg of retinol was formerly assumed to be biologically equivalent to 6.0 μg of β -carotene, but this figure has now been revised upwards [1]. This formula is an approximation that takes into account the inefficiency of conversion of carotenoid to vitamin A as well as the inefficiency of absorption of carotenoids [3].

The UK Food Standards agency states that an average adult should not consume more than 1500 micrograms (5000 IU) per day, because this increases the chance of developing osteoporosis [4].

Vitamin A and the eye

Many of the cells in the retina are "rods" or "cones". Circulating retinol-retinol binding protein complex is required in the formation of rhodopsin (which is *cis*-retinal bound to the vision protein opsin), a membrane protein of the rod cell photoreceptors in the retina. In response to light energy the *cis*-retinal in rhodopsin is converted to *trans*-retinal; the altered shape of the molecule triggers a nerve impulse from the retina

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which is perceived as light in black and white vision. Cone cells, in contrast, are important for colour vision and for bright light vision; they contain retinal-based chromophores that respond to specific wavelengths of light. The immediate time after seeing a flash of bright light involves a period of active rhodopsin synthesis and requires a relatively high level of vitamin A in the retina. "Night blindness" is one of the first detectable signs of vitamin A deficiency. In this condition the blood supplying rod cells contains insufficient *cis*-retinal to rapidly replace the *trans*-retinal formed after exposure to bright light and the resulting condition is called night blindness. If unchecked, the next stage in this process is xeropthalmia, which occurs when the soft, lubricated membrane of the eye transforms into a dry, keratinised epithelium. Xeropthalmia results in total blindness and while this condition is not found in the UK population, it is a common cause of blindness in developing countries, particularly amongst children [1].

Participation in the visual cycle is considered to be the most significant physiological function of *all-trans-retinol*, the predominant form of vitamin A in the circulation. Night blindness was described in Egypt around 1500 BC and Hippocrates later suggested eating liver as a cure for the condition. George Wald won the 1967 Nobel Prize in Physiology for his work on visual pigments, which led to an understanding of the role of vitamin A in vision [5].

Non-visual functions of vitamin A

Many of the non-visual functions of vitamin A are mediated by retinoic acid, which regulates gene expression by activating intracellular retinoic acid receptors. The non-visual functions of vitamin A are essential in the immunological function, reproduction and embryonic development of vertebrates as evidenced by the impaired growth, susceptibility to infection and birth defects observed in populations receiving suboptimal vitamin A in their diet [2].

Vitamin A deficiency also has profound effects on the immune system, but these effects are very selective; with poor vitamin A availability some antigens elicit a poor immune response, while stimulation by other antigens is unaffected. There are also effects on differentiation and stimulation of phagocytosis, as well as modulation of cytokines and eicosanoids [3].

Vitamin A in serum

Serum levels of vitamin A usually remain constant over a wide range of intakes and are largely a reflection of liver stores of retinyl esters [6]. Once on a vitamin A–depleted diet it may take as long as two years for deficiency symptoms to become apparent. Since vitamin A use and disposition depends on retinol binding protein (RBP) as a carrier, so a lack of this protein can also have an impact on vitamin A levels in the circulation.

Audit of approximately 10,000 vitamin A reports by Biolab over the last decade reveals a normal distribution of values with a median serum retinol value of 1.95 μmol/L and a range from 0.19 to 5.60 μmol/L. 2.5 % of these values fall below the reference interval, suggesting vitamin A deficiency in these cases. 20% of the values have exceeded the upper limit, which Biolab has quoted as 2.45 μmol/L. In the light of current authoritative population data [7,8] it has been decided to adopt a new reference interval for serum retinol of **1.05 - 2.80 μmol/L**. Even though the higher values being recorded may reflect vitamin A supplementation and a degree of adiposity in our patient population, it is clear that there is no adverse health effect from increasing circulating retinol from 2.45 μmol/L to 2.80 μmol/L.

Patient preparation

No special preparation is required and the patient can continue to take nutritional supplements and medication before the collection of the sample.

Specimen requirements

Serum or plasma may be used, but special care should be taken to avoid exposure to excess light (which can cause vitamin A to degrade). Specimens should be wrapped in aluminium foil if exposure to natural light cannot be avoided. Separated specimens are stable for 4 weeks at 4°C and for 1 year at -20°C.

Specimens submitted for nutritional assessment of vitamin A should be taken after an overnight fast.

Methodology

Biolab measures vitamin A by a high pressure liquid chromatography technique that is specific for *all-trans-retinol*, the predominant form of vitamin A in the circulation [9].

Turn around time: 5 working days.

References:

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