

M.A. Livrea: Vitamin A and Retinoids: An Update of Biological Aspects and Clinical Applications. Basel, Boston, Berlin: Birkhäuser; 2000. 312 pages; ISBN 3-7643-5882-3; price: DM268.00

Even ancient Egyptians recognized that liver extracts contain something that cures night blindness and other eye disorders. But it was not before the beginning of the 20th century that people resolved the puzzle and named it vitamin A.

Today everybody talks and knows everything about magic substances – vitamins. Many people, trying to stay forever young and healthy, consume enormous quantities of colorful vitamin tablets in every possible combination and amount. But are they right?

Dr Maria A. Livrea from the University of Palermo, Italy, along with many other contributors in her new book, showed us the world of biological aspects and clinical applications of vitamin A and retinoids.

The book consists of a number of review articles illustrated with 42 figures and 23 tables. It is written in an easy-to-read but still very scientific English language and it succeeds in providing us with a full insight into the current knowledge in this field. It is aimed not only at experts in this area but at every curious scientist, student, and medical practitioner wishing to enlarge his/her knowledge and get new ideas for future investigations.

The first three chapters of the book present chemistry and nomenclature of vitamin A in detail, factors affecting blood level of vitamin A, enzymology and biogenesis of retinoic acid, requirements and safety of vitamin A in humans. The International Units (IU) system is used only for synthetic supplements of vitamin A, whereas the REQ (mg retinol equivalents) system is used for dietary intakes of vitamin A. The assessment of the vitamin A status in individuals is classified into 5 categories: deficient, marginal, satisfactory, excessive, and toxic (acute, chronic, and teratogenic). Dietary carotenoids tend to show little, if any, toxicity in humans. Supplements of b-carotene, when taken in large doses over considerable period, can show adverse effects on liver already damaged by alcohol, and lungs damaged by smoking.

The fourth chapter informs us in detail about biology, epidemiology, and trials of carotenoids. They are the best quenchers of $1O_2$ in the nature – each carotenoid molecule can quench 1,000 $1O_2$ molecules before it reacts chemically, thus serving as a very effective antioxidant. Additionally, they interfere with radical-initiated reactions, particularly with those that result in lipid peroxidation. At 100% oxygen, carotenoids act completely opposite – as prooxidants. Many epidemiological studies indicate that persons who consume greater quantities of b-carotene from fruit and vegetables are at lower risk for chronic diseases, especially for lung cancer!

The next chapters give us other strong proofs of important roles of vitamin A and retinoids in many different processes in human organism, such as visual transduction, skin diseases, immunological reactions, infectious diseases, hemopoiesis, carcinogenesis, embryogenic development, and the metabolism of vitamin A and retinoids themselves. But the saying, that there are two sides to a coin is confirmed in the case of vitamin A, too. Connection between embryo malformation and isotretinon (Accutane) usage (for acne treatment during or short time before pregnancy) was reported. These malformations were major, such as hydrocephalus, cardiovascular, and ear defects. At the same time, maternal retinoid deficiency increases the risk of embryonic and fetal demise and precipitates retarded intrauterine growth. That is why the whole chapter is dedicated to the synthetic retinoids and their use and usefulness in the biology and clinical medicine.

In the greater portion of the book, authors attempt to explain in detail possible mechanisms of action of retinoids on fundamental cellular processes including proliferation, differentiation, apoptosis, and malignant transformation. Retinoids inhibit the proliferation and colony formation in various transformed cell lines, including promyelocytic and premonocytic leukemias, embryonal carcinoma, neuroblastoma, melanoma, rhabdomyosarcoma, and breast carcinoma. Since they can restore regulation of premalignant and malignant cell differentiation and growth in vitro and in vivo, certain retinoids are studied as therapeutic and chemopreventive agents for a variety of cancers. The problem of photoaged skin – the effects of the chronic UV radiation (200 to 400 nm) on the skin which are superimposed on the intrinsic aging process – is also included in this valuable book. Clinical features of photoaging are skin roughness, wrinkles, sallowness, mottled hyper- and hypopigmentation, lentigines, telangiectasias, skin laxity, pre-malignant lesions (actinic keratosis, lentigo maligna), and skin cancers (basal cell carcinoma and melanoma). Topical tretinoin application can reverse many aspects of the photoaging process by binding to the nuclear RA receptor (RAR) and forming the complex RA-RAR. This complex binds to the promotor region of the target gene, possibly gene for the procollagen type I. The other possible mechanism of tretinoin effect is inhibition of matrix

metallo-proteinases (collagenase) and blocking the induction of the UV-induced AP-1 transcription factor.

As we can see, in solving the mystery of vitamin A, we got much further than the ancient Egyptians. However, every new insight implies thousands of new questions, which have to be answered. Every new idea is welcome and this book gives us excellent guidelines for finding the way out from the labyrinth we are still in. This significant volume successfully integrates knowledge of basic sciences with clinical practice and it keeps its original promise to be of immense usability for all those whose everyday work is connected with life sciences, from a first-year student to the university professor.

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