age and DHEAS levels was demonstrated in SDAT and healthy elderly subjects. The decrease in 24-hour DHEAS secretion was associated with a higher NK cytotoxic response to DHEAS in the healthy elderly subject group than in healthy subjects of young age. Increased NK cell activity was found in patients with SDAT in comparison with the healthy elderly subject. On the contrary, NK cell cytotoxic response of SDAT patients was less pronounced during DHEAS exposure and when DHEAS was coincubated with IL-2. These data suggest a role of DHEAS in the immune system on NK functional activity in physiological aging and SDAT. Thus, DHEAS has a reducing effect on the overactivity of natural killer immune cells during exposure with cytokines. This effect of DHEAS might stop the pathogenesis and progression of disease by counteracting related neuroimmune components.

*DEMENTIA AND GERIATRIC COGNITIVE DISORDERS, 1999, Vol 10, Iss 1, pp 21-27*

**Grape seed extract weakens development of atherosclerosis**

The aim of this study was to evaluate the antiatherosclerotic effect of proanthocyanidin-rich extracts from grape seeds in cholesterol-fed rabbits. Feeding proanthocyanidin-rich extracts (0.1 and 1% in the diet) to rabbits significantly reduced severe atherosclerosis in the aorta. Immunohistochemical analysis revealed a decrease in the number of oxidized LDL-positive macrophage-derived foam cells in atherosclerotic lesions in the aorta of rabbits fed proanthocyanidin-rich extract. When proanthocyanidin-rich extract was administered orally to rats, proanthocyanidin was detected in the plasma. In an in vitro experiment using human blood, proanthocyanidin-rich extract, which was added to the blood, inhibited the oxidation of LDL. These results suggested that proanthocyanidins, the major polyphenols in red wine, might trap free radicals in blood and interstitial fluid of the arterial wall, thereby inhibiting oxidation of LDL and showing an antiatherosclerotic activity.

*ATHEROSCLEROSIS, 1999, Vol 142, Iss 1, pp 139-149*

**Selenium, vitamin E and defense against viruses**

It has been thought that the immune system is affected by the association between viral disease and nutrition. The theory suggests that because of malnourishment, the immune system is compromised, and there will be an increased susceptibility to viral infection. However, the virus itself may also be affected by the nutritional status. A study showed that a normally benign virus strain becomes virulent (dangerous) in either selenium-deficient or vitamin E-deficient mice. In addition to the deficient animals' immune systems being suppressed, the virus itself is also altered. Changes were found in the virus that replicated in the deficient mice, and once these mutations occurred, even mice with normal nutrition became susceptible to disease. Thus, the poor nutritional status of the individual was able to transform a non-virulent virus into a virulent one due to genetic changes in the virus. An underlying cause of these genetic changes may be common stress from free radicals. The study shows the importance of individual nutrition during a viral disease, not only from the perspective of the individual, but from the perspective of the virus as well.

*PROCEEDINGS OF THE NUTRITION SOCIETY, 1999, Vol 58, Iss 3, pp 707-711*

**The IGF-I response to very low GH doses in human aging**

The activity of the growth hormone (GH)/IGF-I axis varies during life and is reduced in the elderly. In fact, GH, and IGF-I levels in older people are similar to those observed in patients with GH deficiency. The declining activity of the GH/IGF-I axis with advancing age may contribute to changes in body composition, structure, function and metabolism. In fact, treatment with pharmacological doses of GH restored plasma IGF-I levels, increased lean body mass and muscle strength while decreased adipose (fat) tissue mass in healthy elderly subjects. This study aimed to verify the effect of both single dose (Group 1: 20 μg/kg) and short term treatment with very low GH doses (5 μg/kg for 4 days) on the IGF-I levels in 27 normal elderly subjects. Normal young adults (age 21) were studied as controls. The starting IGF-I levels were lower in elderly group than in young group (123.1 vs. 230.4 μg/l). In Group 1, the single administration of 20 μg/kg GH induced a significant IGF-I rise both in young (318.0 vs. 256.0 μg/l) and elderly (187.2 vs. 100.4 9.5 μg/l). IGF-I levels after GH in elderly persisted lower than those in young, but the percentage IGF-I increase after GH was higher in elderly (91.6%) than in young (23.9%) subjects. In Group 2, IGF-I levels were significantly increased 12 hours after the first administration of 5 μg/kg GH both in elderly (166.6 vs. 138.3 μg/l) and young (272.2 vs. 230.4 μg/l). Twelve hours after the last GH administration, IGF-I levels were further increased both in elderly (to 208.7 μg/l) and in young (to 301.7 μg/l). IGF-I levels in elderly persisted lower than those in young at each time point; however, the percentage IGF-I increase after GH in elderly and young was similar (after the
first administration: 22.4% vs. 21.7%; after the last administration: 52.9% vs. 39.5%). The data demonstrate that IGF-I levels in aging are reduced but the peripheral sensitivity to GH is preserved. In fact, in aged subjects the percentage GH-induced IGF-I increase is similar to or higher than that in young controls. The findings also indicate that a very low GH dose is needed in aged subjects to restore IGF-I levels to the young range.

CLINICAL ENDOCRINOLOGY, 1998, Vol 49, Iss 6, pp 757-763

Prevention or reversal of long-term depression by pregnenolone sulfate

The present study investigated the possible relation between long-term depression and barbiturates/benzodiazepine-induced amnesia and attempted to determine the possible effect of pregnenolone sulfate on long-term depression. Results showed long-term depression was either blocked or reversed by pregnenolone sulfate at concentrations (10 μM). The results suggest that the response of this type of long-term depression by benzodiazepines and barbiturates can explain the main adverse effect of these drugs, amnesia and cognitive impairment. Thus, the prevention or reversal of this type of long-term depression by pregnenolone sulfate, may suggest a clinical application of this agent in the management of amnesia or dementia.

PHARMACOLOGICAL RESEARCH, 1998, Vol 38, Iss 6, pp 441-448

Synergistic inhibition of prostate cancer

Retinoic acid and vitamin D3 have demonstrated significant capacity to control proliferation in vitro of many solid tumors. Cooperative synergistic effects by these two have been reported. It is, therefore, possible that greater therapeutic effects could be achieved if these compounds were administered together. The role of retinoid-dependent protein 1 in controlling cancer cell proliferation appears significant. Researchers utilized a retinoid, and a potent vitamin D3 analogue together at low, physiologically safer doses against a panel of prostate cancer cells. The cell lines were synergistically inhibited in their clonal growth by the combination, whereas retinoic acid alone was essentially inactive. Cancer cells underwent apoptosis in the presence of retinoic acid and vitamin D3. The data suggest the retinoid and the vitamin D3 analogue may naturally act synergistically to control cell proliferation, a process that is interrupted during transformation, and that this combination may form the basis for treatment of some androgen-independent prostate cancer.


The Life Extension Foundation honors the National Parkinson Foundation, Inc. and Dr. Deborah C. Mash for their continued efforts to find a cure for Parkinson’s Disease

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Dr. Mash serves as a scientific advisor to the Life Extension Foundation. The Life Extension Foundation is a membership organization dedicated to finding scientific methods of treating and preventing the diseases and effects of aging.