

LE Magazine July 2003

ABSTRACTS

I3C

Chemoprevention of colon cancer by Korean food plant components.

Inducible cyclooxygenase (COX-2) and inducible nitric oxide synthase (iNOS/NOS-2) play pivotal roles as mediators of inflammation involved in early steps of carcinogenesis in certain organs. Therefore, chemoprevention is theoretically possible through inhibition of COX-2 and/or iNOS. In the present study, we examined the chemopreventive effects of indole-3-carbinol (I3C), a constituent of cruciferous vegetables (the family of Cruciferae) such as cabbages, cauliflowers and broccoli on the multiple intestinal neoplasia (Min) genetic mouse model, and on mouse colon carcinogenesis induced by azoxymethane (AOM). The consumption of cruciferous vegetables such as cabbage, broccoli, and Brussels sprouts has been shown to have cancer chemopreventive effects in humans and experimental animals. I3C has been shown to exert a cancer chemopreventive influence in liver, colon, and mammary tissue when given before or concurrent with exposure to a carcinogen. Powdered AIN-76A diets (Harlan Teklad Research Diet, Madison, USA) containing 100 or 300 ppm I3C (group 1 or 2) or the same pellet diets without supplement (group 3) were fed to six-week-old male C57BL/6J-Apc(Min)(/+) (Min/+) mice (The Jackson Laboratory, Bar Harbor, ME, USA) for 10 weeks. In addition the same diets were given to wild-type normal C57BL/6J-Apc(Min)(/+) littermates after AOM initiation (groups 4-7: 10 mice in each group) for 32 weeks from week four. At 16 weeks of age, all Min/+ mice (groups 1-3) were sacrificed for assessment of intestinal polyp development. The incidences of the colonic adenomatous polyps in the groups 1-3 were 60% (12/20), 60% (15/25) and 84% (21/25), respectively. A decreasing tendency in multiplicities of the colonic adenomatous polyps in group 1 (I3C 100 ppm; 0.85 +/- 0.22; 61%) and group 2 (I3C 300 ppm; 1.32 +/- 0.28; 94%) was observed when compared with group 3 (control; 1.40 +/- 0.21; 100%). Total number of aberrant crypt foci (ACF)/colon or aberrant crypts (AC)/colon in wild-type mice of group 4 or 5 were decreased significantly compared with those of the AOM alone group (group 6) (P < 0.01). These results suggest that I3C may be a potential chemopreventive agent for colon cancer.

Mutat Res 2003 Feb-Mar;523-524:99-107

Modulation of vinca-alkaloid induced P-glycoprotein expression by indole-3-carbinol.

The over-expression of *mdr-1* gene transcript P-glycoprotein (P-gp), responsible for multiple drug resistance, is one of the major obstacles in cancer chemotherapy. In the present study, indole-3-carbinol (I3C), a well-known chemopreventive agent present in cruciferous vegetables, has been evaluated for its potential to modulate the over-expression of P-gp induced by vinblastine or vincristine, which are known inducers of *mdr-1* gene. The results revealed that I3C significantly reversed the over-expression of P-gp in vinca-alkaloid induced drug resistance as evident by Western blotting using monoclonal antibody (clone JSB1). Quantization of immunostained tissue sections using image analysis technique revealed that vinblastine/vincristine induced overexpression of P-gp was effectively reversed by I3C. The present investigation suggests that I3C can significantly inhibit the P-gp over-expression and may have utility as a dietary adjuvant in the treatment of cancer for the reversal of multiple drug resistance.

Cancer Lett 2003 Jan 28;189(2):167-73

Serum total homocysteine increases with the rapid proliferation rate of tumor cells and decline upon cell death: a potential new tumor marker.

BACKGROUND: We were interested to know why cancer patients are frequently associated with elevated circulating total homocysteine (tHcy) even though they are not treated with anti-folate drugs. **METHODS:** We employed tissue cultures to compare both the homocysteine (Hcy)-released and production of tumor markers between tumor and normal cell lines. **RESULTS:** We detected much higher concentrations of homocysteine (Hcy) released by the tumor cells. However, much less difference was found between normal and tumor cell lines when Hcy concentration was expressed per the same number of cells. During the cell culture, the increase of Hcy and the increase of tumor marker concentration paralleled each other for the first seven days. After the seventh day of the culture when cells started dying, tumor markers continued to rise, whereas levels of Hcy and cell numbers leveled off. We found that the serum concentration of Hcy fluctuated in circulation coinciding with that of tumor marker in individual cancer patients unless taking anti-neoplastic drug. **CONCLUSIONS:** The elevation of tHcy concentration may be caused by the rapid tumor cell proliferation and reflect only the number of live cells. Serum Hcy may be a potentially useful tumor marker to monitor tumor activity.

Effect of some indole derivatives on xenobiotic metabolism and xenobiotic-induced toxicity in cultured rat liver slices.

In this study the effect of some indole derivatives on xenobiotic metabolizing enzymes and xenobiotic-induced toxicity has been examined in cultured precision-cut liver slices from male Sprague-Dawley rats. While treatment of rat liver slices for 72 hours with 2-200 microM of either indole-3-carbinol (I3C) or indole-3-acetonitrile (3-ICN) had little effect on cytochrome P-450 (CYP)-dependent enzyme activities, enzyme induction was observed after in vivo administration of I3C. The treatment of rat liver slices with 50 microM 3,3'-diindolylmethane (DIM; a dimer derived from I3C under acidic conditions) for 72 hours resulted in a marked induction of CYP-dependent enzyme activities. DIM appears to be a mixed inducer of CYP in rat liver slices having effects on CYP1A, CYP2B and CYP3A subfamily isoforms. Small increases in liver slice reduced glutathione levels and glutathione S-transferase activity were also observed after DIM treatment. While aflatoxin B1 and monocrotaline produced a concentration-dependent inhibition of protein synthesis in 72-hour-cultured rat liver slices, cytotoxicity was markedly reduced in liver slices cultured with 50 microM DIM. These results demonstrate that cultured rat liver slices may be employed to evaluate the effects of chemicals derived from cruciferous and other vegetables on CYP isoforms. In addition, liver slices can also be utilized to examine the ability of such chemicals to modulate xenobiotic-induced toxicity.

Food Chem Toxicol 1999 Jun;37(6):609-18

Prevention of chromosomal aberration in mouse bone marrow by indole-3-carbinol.

In this study, we report the protective effect of indole-3-carbinol (I3C), one of the glucobrassicin derivative isolated from cruciferous vegetables against cyclophosphamide-induced chromosomal aberrations in mouse bone marrow cells. The three test doses namely 1000, 500 and 250 mg/kg b.wt. of I3C provided protection when given 48 h prior to the single i.p. administration of cyclophosphamide (50 mg/kg). I3C alone did not induce chromosomal aberrations at the test doses of 1000 and 500 mg/kg b.wt. Thus, tested glucobrassicin derivative seems to have a preventive potential against cyclophosphamide induced chromosomal aberrations in Swiss mouse bone marrow cells at the doses tested.

Toxicol Lett 1999 Jun 1;106(2-3):137-41

Serum folate, homocysteine and colorectal cancer risk in women: a nested case-control study.

Accumulating evidence suggests that folate, which is plentiful in vegetables and fruits, may be protective against colorectal cancer. The authors have studied the relationship of baseline levels of serum folate and homocysteine to the subsequent risk of colorectal cancer in a nested case-control study including 105 cases and 523 matched controls from the New York University Women's Health Study cohort. In univariate analyses, the cases had lower serum folate and higher serum homocysteine levels than controls. The difference was more significant for folate ($P < 0.001$) than for homocysteine ($P = 0.04$). After adjusting for potential confounders, the risk of colorectal cancer in the subjects in the highest quartile of serum folate was half that of those in the lowest quartile (odds ratio, OR = 0.52, 95% confidence interval, CI = 0.27-0.97, P -value for trend = 0.04). The OR for the highest quartile of homocysteine, relative to the lowest quartile, was 1.72 (95% CI = 0.83-3.65, P -value for trend = 0.09). In addition, the risk of colorectal cancer was almost twice as high in subjects with below-median serum folate and above-median total alcohol intake compared with those with above-median serum folate and below-median alcohol consumption (OR = 1.99, 95% CI = 0.92-4.29). The potentially protective effects of folate need to be confirmed in clinical trials.

Br J Cancer 1999 Apr;79(11-12):1917-22

The effect of indole-3-carbinol and sulforaphane on a prostate cancer cell line.

BACKGROUND: Cruciferous vegetable consumption is inversely related to the incidence of prostate cancer. We examined the effect of indole-3-carbinol (I3C) and of sulforaphane (constituents of cruciferous vegetables) on cell proliferation of a PC-3 prostate cancer cell line, in order to observe if an inhibitory effect might be detected in vitro. **METHODS:** PC-3 prostate cancer cells were cultured in 96-well microtitre plates. Indole-3-carbinol concentrations ranging from 0.1 mmol/L to 0.8 mmol/L or sulforaphane concentrations ranging from 0.01 mmol/L to 0.06 mmol/L were added to the wells. Cell proliferation was measured by colorimetric assay and results were based on the mean value of triplicate experiments. Data are presented as medians and interquartile ranges and were analysed using the Mann-Whitney U-test. **RESULTS:** Cell proliferation in PC-3 prostate cancer cells was significantly inhibited by I3C and sulforaphane at media concentrations of 0.2 mmol/L and 0.02 mmol/L, respectively. **CONCLUSION:** Both compounds inhibited the proliferation of prostate cancer cells in a dose-dependant manner. These findings may help explain the observed protective effect of cruciferous vegetables in relation to prostate cancer.

ANZ J Surg 2003 Mar;73(3):154-6

[Back to the Magazine Forum](#)

ABSTRACTS

Male Fertility

Economics of treatments for male infertility.

Economic factors play a major role in the consideration of treatment options for male reproduction. This article has summarized the data and provided new insight into how patients, insurers and populations evaluate competing therapies for male infertility. Many studies are difficult to interpret because of differing success rates and monetary bias. Future studies comparing line-by-line costs and reimbursements by independent sources may be the best way to evaluate different treatments. *Urol Clin North Am* 2002 Nov;29(4):841-53

Effects of testosterone plus medroxyprogesterone acetate on semen quality, reproductive hormones and germ cell populations in normal young men. Testosterone (T) treatment suppresses gonadotropin levels and sperm counts in normal men, but the addition of a progestin may improve the efficacy of hormonal contraception. This study aimed to investigate the speed and extent of suppression of testicular germ cell number induced by T plus or minus progestin treatment and correlate these changes with serum gonadotropins and inhibin B levels, testicular androgens and sperm output. Thirty normal fertile men (31-46 yr) received either testosterone enanthate (TE, 200 mg im weekly) alone or TE plus depot medroxyprogesterone acetate (DMPA, 300 mg im once) for 2, 6, or 12 wk (n = 5 per group) before vasectomy and testis biopsy. Five men (controls) proceeded directly to surgery. The inclusion of DMPA led to a more rapid fall in serum FSH/LH levels (time to 10% baseline: FSH; 12.6 +/- 2.6 vs. 7.9 +/- 1.4 d; LH, 9.9 +/- 3.4 vs. 3.4 +/- 1.7 d, TE vs. TE+DMPA, respectively, mean +/- SD, both P < 0.0001), yet the mean time to reach a sperm count 10% of baseline was not different (23.7 +/- 7.3 vs. 25.3 +/- 13.9 d, NS). The maximum extent of FSH/LH suppression was identical at 12 wk (mean serum FSH 1.2 and 1.6%, and mean LH 0.3 and 0.2% of baseline: TE vs. TE+ DMPA, respectively) as was sperm count suppression (5 of 5 and 4 of 5 men, respectively, with sperm counts $\leq 0.1 \times 10^6/ml$). Serum inhibin decreased to 55% control at 12 wk in the TE+DMPA group (P < 0.05) but was unchanged by TE treatment (86% control, NS). Testicular T levels declined to approximately 2% of control levels, but testicular dihydrotestosterone and 5alpha-androstane-3alpha,17beta-diol (Adiol) levels were not different to control. Germ cell numbers as determined by stereological methods did not differ between TE and TE+DMPA except at 2 wk when type B spermatogonia and early spermatocytes were significantly lower in the TE+DMPA group (P < 0.05). In all groups, a marked inhibition of Apale- β spermatogonial maturation was seen along with a striking inhibition of spermiation. We conclude that: 1) the addition of DMPA hastens the onset of FSH/LH suppression, correlating with a more rapid impairment of spermatogonial development, but in the longer term, neither germ cell number nor sperm count differed; 2) testicular dihydrotestosterone and Adiol levels are maintained during FSH/LH suppression despite markedly reduced T levels suggesting up-regulation of testicular 5alpha-reductase activity; and 3) spermatogonial inhibition is a consistent feature, but spermiation inhibition is also striking and is an important determinant of sperm output.

J Clin Endocrinol Metab 2002 Feb;87(2):546-56

Comprehensive office evaluation in the new millennium.

The success of a comprehensive office-based evaluation of male-factor infertility depends on the physician's thorough understanding of risk assessment in the history, identification of pertinent physical examination findings and correct assessment of laboratory data. Office-based ultrasonographic techniques have already increased the urologist's ability to visualize suspected anatomic abnormalities, and the use of functional tests of sperm has given greater depth to the limited, but essential, prognostic capabilities of the routine semen analysis.

Urol Clin North Am 2002 Nov;29(4):873-94

The effect of coenzyme Q10 on sperm motility and function.

In sperm cells, the majority of coenzyme Q10 (CoQ10) an energy promoting agent and antioxidant, is concentrated in the mitochondria of the midpiece, so that the energy for movement and all other energy-dependent processes in the sperm cell also depend on the availability of CoQ10. The reduced form of CoQ10-ubiquinol also acts as an antioxidant, preventing lipid peroxidation in sperm membranes. The objective of the study was to evaluate the effect of CoQ10 on sperm motility in vitro, after incubation with 38 samples of asthenospermic and normal motility sperm, and to evaluate the effect of CoQ10 administration in vivo in 17 patients with low fertilization rates after in vitro fertilization with intracytoplasmic sperm injection (ICSI) for male factor infertility. All 38 sperm samples from patients registered in our infertility clinic had normal concentrations and morphology. Of these, 16 patients had normal motility (mean 47.5%) and 22 patients were asthenospermic (mean motility 19.1%). Sperm samples were divided into four equal parts and incubated for 24 h in: HAM's medium alone, in HAM's medium with 1% DMSO and HAM's with 5 microM or 50 microM CoQ10. While no significant change in motility after incubation was observed in the samples with initial normal motility, a significant increase in motility was observed in the 50 microM CoQ10 subgroup of sperm from asthenospermic men, with a motility

rate of 35.7 +/- 19.5%, as compared to 19.1 +/- 9.3% in the controls (P < 0.05). The 17 patients with low fertilization rates after ICSI were treated with oral CoQ10, 60 mg/day, for a mean of 103 days before the next ICSI treatment. No significant change was noted in most sperm parameters, but a significant improvement was noted in fertilization rates, from a mean of 10.3 +/- 10.5% in their previous cycles, to 26.3 +/- 22.8% after CoQ10 (P < 0.05). In conclusion, the administration of CoQ10 may result in improvement in sperm functions in selective patients. Further investigation into the mechanisms related to these effects is needed.

Mol Aspects Med 1997;18 Suppl:S213-9

Lipid peroxidation and human sperm motility: protective role of vitamin E.

Asthenospermia is the main factor of male infertility among patients consulting the Asir Infertility Center in Abha, Saudi Arabia. Lipid peroxidation occurring in both the seminal plasma and spermatozoa was estimated by malondialdehyde (MDA) concentration. Spermatozoal MDA concentration was higher in men with decreased sperm motility. The MDA concentration in the seminal plasma exhibited no relationship with sperm concentration, sperm motility, the number of immotile spermatozoa, or even the absence of spermatozoa. The MDA concentration in sperm pellet suspensions of asthenospermic and oligoasthenospermic patients was almost twice that of the normospermic males. The MDA concentration in the sperm pellet suspension from normospermic or oligospermic patients was about 10% that in the seminal plasma. However, the MDA concentration in the sperm pellet suspension of asthenospermic or oligoasthenospermic patients was about 15% that in the seminal plasma. Treatment of asthenospermic patients with oral Vitamin E significantly decreased the MDA concentration in spermatozoa and improved sperm motility. Eleven out of the 52 treated patients (21%) impregnated their spouses; nine of the spouses successfully ended with normal term deliveries, whereas the other two aborted in the first trimester. No pregnancies were reported in the spouses of the placebo-treated patients.

J Androl 1996 Sep-Oct;17(5):530-7

Testicular function in asymptomatic chronic alcoholics: relation to ethanol intake.

To evaluate the effect of ethanol on testicular function in chronic alcoholics without chronic liver disease, we studied 38 asymptomatic chronic alcoholics and 19 age-matched controls. Detailed clinical history, nutritional status, hormonal analysis, and seminal studies were conducted in each case and control. Alcoholic patients had an average of 39 +/- 2 years old (range: 26 to 60) and reported a daily ethanol consumption from 100 to 350 g (mean: 198 +/- 15) over a period of 18.0 +/- 1.2 years. Alcoholics exhibited a significant increase of the luteinizing hormone (p < 0.001) and a decrease of the Free Androgen Index, compared with controls (p < 0.05) that related significantly with the total lifetime dose of ethanol (p < 0.01, both). Seminal studies indicate that 39.4% of alcoholics had significantly reduced their spermatozoa count (p < 0.01), whereas significant morphological abnormalities were observed in 44.7% of the alcoholics (p < 0.01). Spermatozoa motility from alcoholics was also found to be altered in half of the patients (p < 0.01). A significant increase of serum luteinizing hormone, follicle-stimulating hormone, and sex hormone binding globulin levels, and a decrease of Free Androgen Index were observed in alcoholics with morphology and motility abnormalities (p < 0.05, all). In multivariate analysis, the only independent factor that determined the alterations in sperm (count, morphology abnormalities, and motility alterations) was the total lifetime of ethanol intake (p < 0.001, all). We conclude that alcoholics frequently develop a situation of primary hypogonadism related to a lifetime of ethanol consumption.

Alcohol Clin Exp Res 1997 Feb;21(1):128-33

The effect of smoking and varicocele on human sperm acrosin activity and acrosome reaction.

Smoking and varicocele are frequent findings in the medical history and physical examination of patients attending andrological outpatient departments. However, data about their influence on human semen parameters, such as sperm concentration and motility, are contradictory. Therefore, the purpose of this study was to examine sperm function (acrosin activity and induction of the acrosome reaction) in smokers (n = 30) and varicocele patients (n = 30) compared with normal fertile donors (n = 20). The acrosome reaction was detected by triple staining after 3 h of incubation at 37 degrees C, followed by treatment with 0.1% dimethylsulphoxide (spontaneous acrosome reaction) and 10 microM calcium ionophore A23187 (induced acrosome reaction) for 1 h at 37 degrees C. Acrosin activity was measured by gelatinolysis. The diameters around the sperm heads after gelatinolysis and the percentages of spermatozoa showing halo formations were evaluated. The inducibility of the acrosome reaction was significantly lower in semen samples from smokers than in those from the fertile group (7.1 +/- 3.2 versus 11.2 +/- 4.0%, P < 0.01), whereas no statistically significant difference was demonstrated in spermatozoa from patients with varicocele (9.3 +/- 4.3%). Both the percentages of spermatozoa with halo formation (53.3 +/- 20.0 versus 76.6 +/- 13.6%, P < 0.05) and the halo diameters (16.1 +/- 6.6 versus 31.0 +/- 14.5 microns, P < 0.001) were significantly lower in the varicocele group than in the samples from fertile men. These data suggest that smoking and varicocele affect sperm function, and that the standard semen parameters alone are insufficient to evaluate the influence of both factors on human male fertility.

Hum Reprod 1995 Dec;10(12):3190-4

Continued on Page 3 of 3

[Back to the Magazine Forum](#)

ABSTRACTS

GPC

Alpha-glycerophosphocholine in the mental recovery of cerebral ischemic attacks. An Italian multicenter clinical trial.

The clinical efficacy and the tolerability of alpha-glycerophosphocholine (alpha-GPC), a drug able to provide high levels of choline for the nervous cells of the brain and to protect their cell walls, have been tested in a clinical open multicenter trial on 2044 patients suffering from recent stroke or transient ischemic attacks. alpha-GPC was administered after the attack at the daily dose of 1000 mg im for 28 days and orally at the dose of 400 mg tid during the following five months after the first phase. The evaluation of the efficacy on the psychic recovery was done by the Mathew Scale (MS) during the period of im drug administration, and using the Mini Mental State Test (MMST), the Crichton Rating Scale (CRS), and the Global Deterioration Scale (GDS) during the following period of oral administration. The MS mean increased 15.9 points in 28 days in a statistically significant way ($p < 0.001$) from 58.7 to 74.6. At the end of the five month oral administration, the CRS mean significantly decreased 4.3 points, from 20.2 to 15.9 ($p < 0.001$); the MMST mean significantly increased ($p < 0.001$) from 21 to 24.3 at the end of the trial, reaching the "normality" score at the 3rd month assessment. The GDS score at the end of the trial corresponded to "no cognitive decline" or "forgetfulness" in 71% of the patients. Forty-four patients complained of adverse events (2.14%); in 14 (0.7%) the investigator preferred to discontinue therapy. The most frequent complaints were heartburn (0.7%), nausea-vomit (0.5%), insomnia-excitation (0.4%), and headache (0.2%). The trial confirms the therapeutic role of alpha-GPC on the cognitive recovery of patients with acute stroke or TIA, and the low percentage of adverse events confirms its excellent tolerability.

Ann N Y Acad Sci 1994 Jun 30;717:253-69

Choline chloride fails to improve cognition of Alzheimer's disease.

Seven mildly- to moderately-demented patients with Alzheimer's disease were treated with either placebo or choline chloride (50, 100 and 200 mg/kg/24 hrs) in a double blind, crossover study. Detailed psychometric analysis was carried out at the end of each two-week period of drug or placebo administration. No subjects showed significant overall improvement at any dose level despite more than a doubling of the baseline plasma choline level.

Neurobiol Aging 1981 Fall;2(3):205-8

Choline alphoscerate in cognitive decline and in acute cerebrovascular disease: an analysis of published clinical data.

This paper has reviewed the documentation on the clinical efficacy of choline alphoscerate, a cholinergic precursor, considered as a centrally-acting parasympathomimetic drug in dementia disorders and in acute cerebrovascular disease. Thirteen published clinical trials, examining in total 4,054 patients, have evaluated the use of choline alphoscerate in various forms of dementia disorders of degenerative, vascular or combined origin, such as senile dementia of the Alzheimer's type (SDAT) or vascular dementia (VaD) and in acute cerebrovascular diseases, such as transitory ischemic attack (TIA) and stroke. Analysis has assessed the design of each study, in particular with respect to experimental design, number of cases, duration of treatment and tests used to evaluate drug clinical efficacy. Most of the ten studies performed in dementia disorders were controlled trials versus a reference drug or placebo. Overall, 1,570 patients were assessed in these studies, 854 of which in controlled trials. As detected by validated and appropriate tests, such as Mini Mental State Evaluation (MMSE) in SDAT and Sandoz Clinical Assessment Geriatric (SCAG) in VaD, administration of choline alphoscerate significantly improved patient clinical condition. Clinical results obtained with choline alphoscerate were superior or equivalent to those observed in control groups under active treatment and superior to the results observed in placebo groups. Analysis stresses the clear internal consistency of clinical data gathered by different experimental situations on the drug effect, especially with regard to the cognitive symptoms (memory, attention) characterizing the clinical picture of adult-onset dementia disorders. The therapeutic usefulness of choline alphoscerate in relieving cognitive symptoms of chronic cerebral deterioration differentiates this drug from cholinergic precursors used in the past, such as choline and lecithin. Three uncontrolled trials were performed with choline alphoscerate in acute cerebrovascular stroke and TIA, totalling 2,484 patients. The results of these trials suggest that this drug might favor functional recovery of patients with cerebral stroke and should be confirmed in future investigations aimed at establishing the efficacy of the drug in achieving functional recovery of patients with acute cerebrovascular disease.

Mech Ageing Dev 2001 Nov;122(16):2041-55

Alpha-glycerolphosphorylcholine administration increases the GH responses to GHRH of young and elderly subjects.

Growth hormone (GH) secretion is decreased during aging in humans and in rodents. This decrease may be due to increased hypothalamic somatostatin release, which is inhibited by cholinergic agonists or to decreased secretion of GHRH. Alpha-glycerylphosphorylcholine (alpha-GFC) is a putative acetylcholine precursor used in the treatment of cognitive disorders in the elderly. In order to learn what effect alpha-GFC had on GH secretion, GH-release hormone (GHRH) was given to young and old human volunteers, with or without the addition of alpha-GFC. GH secretion was greater in the younger subjects than in the old individuals, and both groups had a greater GH response to the GHRH+alpha-GFC than to GHRH alone. The potentiating effect of alpha-GFC on GH secretion was more pronounced in the elderly subjects. These findings confirm the observation that aged individuals respond less well to GHRH than younger subjects, and provides further evidence that increased cholinergic tone enhances GH release.

Horm Metab Res 1992 Mar;24(3):119-21

Long-term choline alfoscerate treatment counters age-dependent microanatomical changes in rat brain.

1. The density of nerve cells and of silver-gold impregnated fibres were evaluated in the hippocampus and in the cerebellar cortex in adult (12-month-old) and old (24-month-old) Sprague-Dawley rats. 2. The effects of long-term choline alfoscerate (GFC) treatment (100 mg/Kg/day for six months) on the above parameters were investigated in old rats. 3. The number of nerve cell profiles and the area occupied by silver-gold impregnated fibres were decreased both in the hippocampus and in the cerebellar cortex in old in comparison with adult rats. 4. GFC treatment countered the age-dependent reduction of nerve cells and silver-gold impregnated fibres. The hippocampus was more sensitive than the cerebellar cortex to the activity of GFC. 5. These results suggest that GFC treatment is effective in slowing down the expression of structural changes occurring in aging brain.

Prog Neuropsychopharmacol Biol Psychiatry 1994 Sep;18(5):915-24

Prevalence of Alzheimer's disease and other dementias in rural India: the Indo-U.S. study.

OBJECTIVE: To determine the prevalence of Alzheimer's disease (AD) and other dementias in a rural elderly Hindi-speaking population in Ballabgarh in northern India. **DESIGN:** The authors performed a community survey of a cohort of 5,126 individuals aged 55 years and older, 73.3% of whom were illiterate. Hindi cognitive and functional screening instruments, developed for and validated in this population, were used to screen the cohort. A total of 536 subjects (10.5%) who met operational criteria for cognitive and functional impairment and a random sample of 270 unimpaired control subjects (5.3%) underwent standardized clinical assessment for dementia using the Diagnostic and Statistical Manual of Mental Disorders-fourth edition diagnostic criteria, the Clinical Dementia Rating Scale (CDR), and National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) criteria for probable and possible AD. **RESULTS:** We found an overall prevalence rate of 0.84% (95% CI, 0.61 to 1.13) for all dementias with a CDR score of at least 0.5 in the population aged 55 years and older, and an overall prevalence rate of 1.36% (95% CI, 0.96 to 1.88) in the population aged 65 years and older. The overall prevalence rate for AD was 0.62% (95% CI, 0.43 to 0.88) in the population aged 55+ and 1.07% (95% CI, 0.72 to 1.53) in the population aged 65+. Greater age was associated significantly with higher prevalence of both AD and all dementias, but neither gender nor literacy was associated with prevalence. **CONCLUSIONS:** In this population, the prevalence of AD and other dementias was low, increased with age, and was not associated with gender or literacy. Possible explanations include low overall life expectancy, short survival with the disease, and low age-specific incidence potentially due to differences in the underlying distribution of risk and protective factors compared with populations with higher prevalence.

Neurology 1998 Oct;51(4):1000-8

Classification criteria for mild cognitive impairment: a population-based validation study

OBJECTIVE: To evaluate the predictive validity and temporal stability of diagnostic criteria for mild cognitive impairment (MCI). **BACKGROUND:** MCI has been proposed as a nosologic entity referring to elderly persons with subclinical cognitive deficits due to incipient dementia. Classification criteria, which have been derived from small, selected clinical groups, are currently disputed, and have not yet been assessed within the general population. **METHODS:** Subjects meeting current criteria for MCI and also age-associated cognitive decline (AACD—a similar concept that is assumed to be related to normal cognitive aging processes rather than incipient dementia) were identified within each of three waves of a longitudinal population study, which included a standardized neurologic examination. **RESULTS:** In the general population, the prevalence of MCI was estimated to be 3.2% and AACD 19.3%. MCI was a poor predictor of dementia within a 3-year period, with an 11.1% conversion rate. Subjects with MCI also constituted an unstable group, with almost all subjects changing category each year. Discriminant function analysis failed to isolate a homogeneous clinical group. Subjects classified as AACD, contrary to the theoretical assumptions underlying the disorder, represented a more stable group, with a 28.6% conversion rate to dementia over three years (relative risk = 21.2). **CONCLUSION:** MCI criteria perform poorly when applied to a representative population sample. The authors propose modifications to current diagnostic criteria to increase their capacity to detect incipient dementia.

Neurology 2001 Jan 9;56(1):37-42

The field of aging and dementia is focusing on the characterization of the earliest stages of cognitive impairment. Recent research has identified a transitional state between the cognitive changes of normal aging and Alzheimer's disease (AD), known as mild cognitive impairment (MCI). Mild cognitive impairment refers to the clinical condition between normal aging and AD in which persons experience memory loss to a greater extent than one would expect for age, yet they do not meet currently accepted criteria for clinically probable AD. When these persons are observed longitudinally, they progress to clinically probable AD at a considerably accelerated rate compared with healthy age-matched individuals. Consequently, this condition has been recognized as suitable for possible therapeutic intervention, and several multicenter international treatment trials are under way. Because this is a topic of intense interest, a group of experts on aging and MCI from around the world in the fields of neurology, psychiatry, geriatrics, neuropsychology, neuroimaging, neuropathology, clinical trials and ethics was convened to summarize the current state of the field of MCI. Participants reviewed the world scientific literature on aging and MCI and summarized the various topics with respect to available evidence on MCI. Diagnostic criteria and clinical outcomes of these subjects are available in the literature. Mild cognitive impairment is believed to be a high-risk condition for the development of clinically probable AD. Heterogeneity in the use of the term was recognized, and subclassifications were suggested. While no treatments are recommended for MCI currently, clinical trials regarding potential therapies are under way. Recommendations concerning ethical issues in the diagnosis and the management of subjects with MCI were made.

Arch Neurol 2001 Dec;58(12):1985-92

[Back to the Magazine Forum](#)

All Contents Copyright © 1995-2009 Life Extension Foundation All rights reserved.

LifeExtension®

These statements have not been evaluated by the FDA. These products are not intended to diagnose, treat, cure or prevent any disease. The information provided on this site is for informational purposes only and is not intended as a substitute for advice from your physician or other health care professional or any information contained on or in any product label or packaging. You should not use the information on this site for diagnosis or treatment of any health problem or for prescription of any medication or other treatment. You should consult with a healthcare professional before starting any diet, exercise or supplementation program, before taking any medication, or if you have or suspect you might have a health problem. You should not stop taking any medication without first consulting your physician.