



RESEARCH UPDATES

For the latest in worldwide integrated cancer care

September 2008



InspireHealth
INTEGRATED CANCER CARE

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Research Updates is produced once a month by InspireHealth to inform those interested of newly published articles in integrative cancer care. Authoritative articles are selected based on their evidence and their relevance to this area of medicine.

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Breast

Ready, A, C. M. Velicer, A. McTiernan and E. White. **NSAID use and Breast Cancer Risk in the VITAL Cohort.** *Breast Cancer Research & Treatment.* 2008 Jun; 109(3): 533-543. **OBJECTIVE:** We prospectively evaluated the association between average 10-year use of NSAIDs and invasive breast cancer. **METHODS:** Between 2000-2002, 35,323 postmenopausal women participating in the Vitamins And Lifestyle (VITAL) study provided detailed information regarding NSAID use, lifestyle and breast cancer risk factors. Using a Cox proportional hazards model, we analyzed associations between NSAID use and incident breast cancer (N = 482) ascertained through linkage to the SEER cancer registry. **RESULTS:** Use of low-dose aspirin at 4+ days/week over ten years was associated with a decreased risk of breast cancer (HR 0.65, confidence interval [CI] 0.43-0.97) versus no use, as was moderate use of other types of NSAIDs (HR 0.78, CI 0.61-0.98) for 10-yr average use up to 3 days/week. However, more frequent use of NSAIDs other than low-dose aspirin was associated with an increased risk (HR 1.26, CI 0.96-1.65), particularly frequent use of regular or extra strength aspirin (HR 1.43, CI 1.02-2.00). **CONCLUSIONS:** We did not find evidence of a global protective effect of NSAID use for the development of breast cancer. However, long-term moderate use (frequent use of low doses or moderate frequency of high doses) was associated with reduced risk, while frequent use of higher dose products was associated with increased risk.

Fenlon, DR, J. L. Corner and J. S. Haviland. **A Randomized Controlled Trial of Relaxation Training to Reduce Hot Flashes in Women with Primary Breast Cancer.** *Journal of Pain & Symptom Management.* 2008 Apr; 35(4): 397-405.

Hot flashes are experienced by about 52% of perimenopausal women. After breast cancer, this may increase to 70%. The use of hormone replacement therapy is not recommended in women who have had breast cancer; therefore, alternatives are required to help relieve hot flashes. This study was conducted to assess the efficacy of relaxation training in reducing the incidence of hot flashes in women with primary breast cancer. This was a randomized controlled trial of 150 women with primary

breast cancer who experienced hot flashes. The intervention group received a single relaxation training session and was instructed to use practice tapes on a daily basis at home for one month; the control group received no intervention. Outcomes were incidence and severity of flashes using a diary and validated measures of anxiety and quality of life. The incidence and severity of hot flashes, as recorded by diaries, each significantly declined over one month (P<0.001 and P=0.01, respectively), compared with the control group. Distress caused by flashes also significantly declined in the treatment group over one month (P=0.01), compared with the control group. There were no significant differences between the treatment group and the control group at three months and no changes in anxiety or quality-of-life measures. Relaxation may be a useful component of a program of measures to relieve hot flashes in women with primary breast cancer.

Kogure, T, K. Ito, H. Sato, et al. **Efficacy of Nyoshinsan/TJ-67, a Traditional Herbal Medicine, for Menopausal Symptoms Following Surgery and Adjuvant Chemotherapy for Premenopausal Breast Cancer.** *International Journal of Clinical Oncology.* 2008 Apr; 13(2): 185-189. We report a 39-year-old woman with premenopausal breast cancer who developed estrogen-deficiency symptoms associated with chemotherapy-related amenorrhea, and was successfully treated with Nyoshinsan/TJ-67, a Japanese traditional herbal medicine (Kampo). Six other breast cancer survivors with menopausal symptoms were also treated with Nyoshinsan/TJ-67, and five of the six patients showed noticeable improvement without adverse effects. Managing estrogen-deficiency symptoms in breast cancer survivors is still problematic, and Nyoshinsan/TJ-67 may be a useful and safe agent for such symptoms in these patients. copyright 2008 Japan Society of Clinical Oncology.

Prostate

Ahn, J, R. Moslehi, S. J. Weinstein, K. Snyder, J. Virtamo and D. Albanes. **Family History of Prostate Cancer and Prostate Cancer Risk in the Alpha-Tocopherol, Beta-Carotene Cancer Prevention (ATBC) Study.** *International Journal of Cancer.* 2008 Sep 1; 123(5): 1154-1159.

Prostate cancer family history has been associated with increased risk of the malignancy. Most prior studies have been retrospective and subject to recall bias, however, and data evaluating interactions with other important risk factors are limited. We examined the relationship between a family history of prostate cancer and prostate cancer risk in relation to body size, micronutrients and other exposures in the Alpha-Tocopherol, Beta-Carotene Cancer Prevention (ATBC) Study cohort of Finnish male smokers. Family history of cancer information was self-reported once during the study in 1991, and anthropometry was measured by trained personnel. Among 19,652 men with complete data, 1,111 incident cases were identified during up to 12.3 years of follow-up. A first-degree family history of prostate cancer was associated with an overall relative risk (RR) of 1.91 (95% CI = 1.49-2.47) and a RR of 4.16 (95% CI = 2.67-6.49) for advanced disease (stage \geq 3), adjusted for age and trial intervention. Our data also suggest that to some degree, height, body mass index, and serum alpha-tocopherol and beta-carotene modify the family history and prostate cancer association, although the interactions were not statistically significant. Supplementation with vitamin E or beta-carotene did not modify the family history-prostate cancer association. This study provides additional evidence that family history is a significant risk factor for prostate cancer.

Park, SY, S. P. Murphy, L. R. Wilkens, B. E. Henderson, L. N. Kolonel and Study Multiethnic Cohort. **Legume and Isoflavone Intake and Prostate Cancer Risk: The Multiethnic Cohort Study.** *International Journal of Cancer.* 2008 Aug 15; 1234: 927-932.

Findings from studies of legume, soy and isoflavone intake and prostate cancer risk are as yet inconclusive, although soy has received considerable attention due to its high phytoestrogen content. Therefore, the present study investigated the relationship of these dietary exposures to prostate cancer risk in the Multiethnic Cohort Study in Hawaii and Los Angeles. The analyses included 82,483 men who completed a detailed quantitative food frequency questionnaire in 1993-1996. A total of 4,404 prostate cancer cases including 1,278 nonlocalized or high-grade cases were recorded during the average follow-up period of 8 years. Multivariate relative risks (RR) and 95% of confidence intervals (CI) were estimated using Cox proportional hazards models with age as the time metric. Among men with the highest intake of legumes, the risk reduction was 11% for total prostate cancer (RR = 0.89, 95% CI = 0.80-0.99, p for trend = 0.007) and 26% for nonlocalized or high-grade cancer (RR = 0.74, 95% CI = 0.61-0.90, p for trend = 0.007) compared to men with the lowest intake. Similar risk reductions were observed for soy products and for legumes excluding soy products in separate analyses. We found no significant risk reduction associated with intake of total or specific isoflavones for either total prostate cancer or for nonlocalized or high-grade cancer. The findings of our study suggest that legume intake is associated with a moderate reduction in prostate cancer risk and that the isoflavones in soy products are probably not responsible for this effect. (c) 2008 Wiley-Liss, Inc.

 Thank you to the **BC Foundation for Prostate Disease** for their generous support.
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Lung

Mahabir, S, K. Schendel, Y. Q. Dong, S. L. Barrera, M. R. Spitz and M. R. Forman. **Dietary Alpha-, Beta-, Gamma- and Delta-Tocopherols in Lung Cancer Risk.** *International Journal of Cancer.* 2008 Sep 1; 1235: 1173-1180. Studies of vitamin E and cancer have focused on the alpha-tocopherol form of the vitamin. However, other forms of vitamin E, in particular gamma-tocopherol may have unique mechanistic characteristics relevant to lung cancer prevention. In an ongoing study of 1,088 incident lung cancer cases and 1,414 healthy

matched controls, we studied the associations between 4 tocopherols (alpha-, beta-, gamma-, and delta-tocopherol) in the diet and lung cancer risk. Using multiple logistic regression analysis, the adjusted odds ratios (OR) and 95% confidence intervals (CI) of lung cancer for increasing quartiles of dietary alpha-tocopherol intake were 1.0, 0.63 (0.50-0.79), 0.58 (0.44-0.76) and 0.39 (0.28-0.53), respectively (p-trend < 0.0001). For dietary intake of beta-tocopherol, the OR and 95% CI for all subjects were: 1.0, 0.79 (0.63-0.98), 0.59 (0.45-0.78) and 0.56 (0.42-0.74), respectively (p-trend < 0.0001). Similar results for dietary gamma-tocopherol intake were observed: 1.0, 0.84 (0.67-1.06), 0.76 (0.59-0.97) and 0.56 (0.42-0.75), respectively (p-trend = 0.0002). No significant association between delta-tocopherol intake and lung cancer risk was detected. When the 4 tocopherols were summed as total tocopherol intake, a monotonic risk reduction was also observed. When we entered the other tocopherols in our model, only the association with dietary alpha-tocopherol intake remained significant; i.e., increasing intake of dietary alpha-tocopherol accounted for 34-53% reductions in lung cancer risk. To the best of our knowledge, this is the first report of the independent associations of the 4 forms of dietary tocopherol (alpha-, beta-, gamma- and delta-tocopherol) on lung cancer risk. Given the limitations with case-control studies, these findings need to be confirmed in further investigations.

Head & Neck

McNeely, ML, M. B. Parliament, H. Seikaly, et al. **Effect of Exercise on Upper Extremity Pain and Dysfunction in Head and Neck Cancer Survivors: A Randomized Controlled Trial.** *Cancer.* 2008 Jul 1; 1131: 214-222. **BACKGROUND:** Shoulder pain and disability are well recognized complications associated with surgery for head and neck cancer. This study was designed to examine the effects of progressive resistance exercise training (PRET) on upper extremity pain and dysfunction in postsurgical head and neck cancer survivors. **METHODS:** Fifty-two head and neck cancer survivors were assigned randomly to PRET (n = 27) or a standardized therapeutic exercise protocol (TP) (n = 25) for 12 weeks. The primary endpoint was change in patient-rated shoulder pain and disability from baseline to postintervention. Secondary endpoints were upper extremity strength and endurance, range of motion, fatigue, and quality of life. **RESULTS:** Follow-up assessment for the primary outcome was 92%, and adherence to the supervised PRET and TP programs were 95% and 87%, respectively. On the basis of intention-to-treat analyses, PRET was superior to TP for improving shoulder pain and disability (-9.6; 95% confidence interval [95% CI], -16.4 to -4.5; P = .001), upper extremity strength (+10.8 kg; 95% CI, 5.4-16.2 kg; P < .001), and upper extremity endurance (+194 repetitions x kg; 95% CI, 10-378 repetitions x kg; P = .039). Changes in neck dissection impairment, fatigue, and quality of life favored the PRET group but did not reach statistical significance. **CONCLUSIONS:** The PRET program significantly reduced shoulder pain and disability and improved upper extremity muscular strength and endurance in head and neck cancer survivors who had shoulder dysfunction because of spinal accessory nerve damage. Clinicians should consider the addition of PRET in the rehabilitation of postsurgical head and neck cancer survivors. (Copyright) 2008 American Cancer Society.

Ovarian

Rossi, M, E. Negri, P. Lagioui, et al. **Flavonoids and Ovarian Cancer Risk: A Case-Control Study in Italy.** *International Journal of Cancer.* 2008 Aug 15; 1234: 895-898. Flavonoids belong to a vast group of polyphenols widely distributed in all foods of plant origin. Because of their antioxidant, antimutagenic and antiproliferative properties, they have been hypothesized to contribute to the favorable effects of fruit and vegetables against cancer. The aim of this study is to investigate the relation of 6 classes of flavonoids (flavan-3-ols, flavanones,

flavonols, flavones, anthocyanidins and isoflavones) with ovarian cancer risk, using data from a multicentric case-control study conducted in Italy between 1992 and 1999. The study included 1,031 cases with incident, histologically confirmed epithelial ovarian cancer and 2,411 controls admitted for acute, nonneoplastic conditions to major hospitals in the same catchment areas. In logistic regression models including study center, education, year of interview, parity, oral contraceptive use and family history of ovarian or breast cancer or both, an inverse relation with significant trend in risk was found between ovarian cancer and flavonols [odds ratio (OR), 0.63; 95% confidence intervals (CI) 0.47-0.84] as well as isoflavones (OR, 0.51; 95% CI, 0.37-0.69), comparing the highest versus the lowest quintile. Further adjustment for fruit and vegetable intake did not modify these associations, suggesting that isoflavones and flavonols may have a distinct role in explaining the effect of fruit and vegetable against ovarian cancer. On the basis of our findings and the relevant literature, we infer that isoflavones, and perhaps flavonols, may have favorable effects with respect to ovarian cancer risk. (c) 2008 Wiley-Liss, Inc.

Song, YJ, A. R. Kristal, K. G. Wicklund, K. L. Cushing-Haugen and M. A. Rossing. **Coffee, Tea, Colas, and Risk of Epithelial Ovarian Cancer.** *Cancer Epidemiology, Biomarkers & Prevention.* 2008 Mar; 173: 712-716. Associations of coffee, tea, and other caffeinated beverages with ovarian cancer risk remain uncertain. In a population-based study in Washington State, 781 women with epithelial ovarian cancer diagnosed in 2002 to 2005 and 1,263 controls completed self-administered questionnaires detailing consumption of caffeinated and noncaffeinated coffee, teas, and colas and in-person interviews regarding reproductive and hormonal exposures. We assessed risk associated with coffee, tea, and cola drinking and with total caffeine consumption using logistic regression to calculate odds ratios and 95% confidence intervals. Neither caffeinated nor decaffeinated coffees were associated with ovarian cancer risk; also, we observed no association of total caffeine with risk using a combined index that summed intake from coffee, tea, and carbonated soft drinks. Among teas, neither herbal/decaffeinated nor black teas were associated with risk; however, women who reported drinking ≥ 1 cup/d of green tea had a 54% reduction in risk (P trend = 0.01). Associations of green tea with risk were similar when invasive and borderline cases were considered separately and when Asian women were excluded from analysis. Green tea, which is commonly consumed in countries with low ovarian cancer incidence, should be further investigated for its cancer prevention properties.

Antioxidants

Liu, BL, X. Zhang, W. Zhang and H. N. Zhen. **New Enlightenment of French Paradox: Resveratrol's Potential for Cancer Chemoprevention and Anti-Cancer Therapy** *Cancer Biology & Therapy.* 2007 Dec; 612: 1833-1836. Resveratrol is a phytoalexin produced by many plants, and the skin of red grapes is particularly rich in resveratrol which accounts for the "French Paradox". Besides its protection of the cardiovascular system, it can affect the processes underlying all three stages of carcinogenesis, involving tumor initiation, promotion and progression. It has also been shown to suppress angiogenesis and metastasis. The anti-carcinogenic effects of resveratrol appear to be closely associated with its capacity to interact with multiple molecular targets involved in cancer development, while minimizing toxicity in normal tissues as tested. By reviewing many in vitro and in vivo studies, also considering both the supporting and challenging evidences, we are provided with a theory in support of the use of resveratrol in human cancer chemoprevention, in combination with either chemotherapeutic drugs or cytotoxic factors for the highly efficient treatment of drug refractory tumor cells. Anti-carcinogenic potential for cancer chemoprevention and anticancer therapy, which is one of the pleiotropic effects of resveratrol, is so called a new enlightenment of French Paradox. [References: 30]

Diet & Nutrition

Benetou, V, A. Trichopoulou, P. Orfanos, et al. **Conformity to Traditional Mediterranean Diet and Cancer Incidence: The Greek EPIC Cohort.** *Br J Cancer.* 2008 08 Jul; 991: 191-195. Adherence to traditional Mediterranean diet (MD) has been reported to be inversely associated with total, as well as cardiovascular, mortality. We have examined the relation between degree of such adherence and incidence of cancer overall in a general population sample of 25 623 participants (10 582 men, 15 041 women) of the Greek segment of the European Prospective Investigation into Cancer and nutrition (EPIC). All subjects completed a validated, interviewer-administered, semi-quantitative food-frequency questionnaire at enrolment. Degree of adherence to the traditional MD was assessed through a 10-point scale (0 minimal; 9 maximal) that incorporated key dietary characteristics. During a median follow-up of 7.9 years and 188 042 total person-years, 851 medically confirmed incident cancer cases (421 men, 430 women) were recorded. Using proportional hazards regression with adjustment for potential confounders, we found that a higher degree of MD adherence was associated with lower overall cancer incidence. A two-point increase in the score corresponded to a 12% reduction in cancer incidence (adjusted hazard ratio, 0.88 (95% confidence interval 0.80, 0.95)). The association was exposure-dependent and stronger among women. This inverse association with MD adherence was considerably stronger than that predicted on the basis of the associations of the individual components of this diet and points to the value of analysing dietary patterns in cancer studies. copyright 2008 Cancer Research UK.

Seki, T, T. Hosono, T. Hosono-Fukao, et al. **Anticancer Effects of Diallyl Trisulfide Derived from Garlic** *Asia Pac J Clin Nutr.* 2008 17Suppl 1: 249-252. Alk(en)yl sulfides are characteristic flavor components of garlic. Several lines of epidemiological study indicate that the risk of a certain cancer can be prevented by consumption of garlic. In this manuscript, we examined the anticancer property of garlic-derived alk(en)yl sulfides, and the molecular basis especially for diallyl trisulfide which is a major constituent of the garlic oil. Alk(en)yl sulfides with different numbers of sulfur atom (i.e., mono-, di-, and trisulfide) were synthesized and purified (>99%). The anticancer activity of the alk(en)yl sulfides was primarily examined using human colon cancer cells HCT-15 and DLD-1. The growth of the cells was significantly suppressed by diallyl trisulfide, but neither diallyl monosulfide nor diallyl disulfide showed such an effect. The number of cells arrested at G2/M phase, the cells with a sub-G1 DNA content, and the cells with caspase-3 activity were dramatically increased by diallyl trisulfide treatment. Diallyl trisulfide disrupted microtubule network formation of the cells, and microtubule fragments could be seen at the interphase. There was a specific oxidative modification of cysteine residues Cys12 beta and Cys354 beta, forming S-allylmercaptocysteines in the tubulin molecule. These results suggest that diallyl trisulfide is responsible, at least in part, for the epidemiologically proven anticancer effect for garlic eaters. [References: 11]

Cutler, GJ, J. A. Nettleton, J. A. Ross, et al. **Dietary Flavonoid Intake and Risk of Cancer in Postmenopausal Women: The Iowa Women's Health Study.** *International Journal of Cancer.* 2008 Aug 1; 1233: 664-671. Flavonoids, which are found in certain plant foods, are thought to lower cancer risk through their antioxidant, antiestrogenic and antiproliferative properties. We examined the association of intake of total flavonoids and 7 flavonoid subclasses with risk of lung, colorectal, breast, pancreatic and upper aerodigestive cancer among women in a large prospective cohort study. Study participants were 34,708 postmenopausal women in the Iowa Women's Health Study who completed a food frequency questionnaire and were followed for cancer occurrence from 1986 through 2004. Flavonoid intake was estimated from 3 databases

developed by the USDA Nutrient Data Laboratory (NDL). Hazard ratios (HR) for cancer risk were calculated across total flavonoid and flavonoid subclass intake categories. Interactions between smoking history and flavonoid intake were also examined. After multivariable adjustment, lung cancer incidence was inversely associated with intakes of flavanones (HR = 0.68; 95% CI: 0.53-0.86, all results highest vs. lowest quintile) and proanthocyanidins (HR = 0.75; 95% CI: 0.57-0.97). Among current and past smokers, those with intakes in the highest quintile for flavanones (HR = 0.66; 95% CI: 0.50-0.86), and proanthocyanidins (HR = 0.66; 95% CI: 0.49-0.89) had significantly lower lung cancer incidence than those in the lowest quintile. Similar associations were not seen in never smokers. Isoflavone intake was inversely associated with overall cancer incidence (HR = 0.93, 95% CI: 0.86-1.00). This study provides further support for a beneficial effect of flavonoid intake on lung cancer risk, especially among current and past smokers.

Lifestyle

Demark-Wahnefried, W, C. L. Rock, K. Patrick and T. Byers. **Lifestyle Interventions to Reduce Cancer Risk and Improve Outcomes.** *Am Fam Physician.* 2008 Jun 1; 77(11): 1573-1578. There are more than one half million cancer deaths in the United States each year, and one third of these deaths are attributed to suboptimal diet and physical activity practices. Maintaining a healthy weight, staying physically active throughout life, and consuming a healthy diet can substantially reduce the lifetime risk of developing cancer, as well as influence overall health and survival after a cancer diagnosis. The American Cancer Society's Nutrition and Physical Activity Guidelines serve as a source document for communication, policy, and community strategies to improve dietary and physical activity patterns among Americans. In 2006, they published updated guidelines for the primary prevention of cancer and guidelines for improving outcomes among cancer survivors through tertiary prevention. These two sets of guidelines have similar recommendations, including: achievement and maintenance of a healthy weight; regular physical activity of at least 30 minutes per day and at least five days per week; a plant-based diet high in fruits, vegetables, and whole grains and low in saturated fats and red meats; and moderate alcohol consumption, if at all. Physicians are encouraged to find teachable moments to impart appropriate nutrition, physical activity, and weight management guidance to their patients, and to support policies and programs that can improve these factors in the community to reduce cancer risk and improve outcomes after cancer. [References: 50]

Vitamin D

Mohr, SB, C. F. Garland, E. D. Gorham, W. B. Grant and F. C. Garland. **Could Ultraviolet B Irradiance and Vitamin D be Associated with Lower Incidence Rates of Lung Cancer?** *Journal of Epidemiology & Community Health.* 2008 Jan; 62(1): 69-74. **BACKGROUND:** This study examines whether insufficient ultraviolet B (UVB) irradiance, a marker of vitamin D inadequacy, might contribute to lung cancer incidence. **METHODS:** The association of latitude and UVB irradiance with age-adjusted incidence rates of lung cancer in 111 countries was investigated. Independent associations with UVB irradiance, cloud cover, anthropogenic aerosols, and cigarette smoking, were assessed using multiple regression. **RESULTS:** Latitude was positively related to incidence rates in men ($R(2) = 0.55, p < 0.01$) and women ($R(2) = 0.36, p < 0.01$). In men, cigarette consumption ($p < 0.001$) was positively related to risk, whereas UVB irradiance was inversely associated ($p = 0.003$). There were positive associations with UVB absorbers, in particular cloud cover ($p = 0.05$) and aerosol optical depth ($p = 0.005$). The $R(2)$ for the model was 0.78 ($p < 0.001$). UVB irradiance was also inversely associated with incidence rates in women ($p = 0.0002$), whereas cigarette consumption ($p < 0.001$), total cloud cover ($p = 0.02$) and aerosol

optical depth ($p = 0.005$) were positively associated. The $R(2)$ for the model was 0.77 ($p < 0.001$). **CONCLUSIONS:** Lower levels of UVB irradiance were independently associated with higher incidence rates of lung cancer in 111 countries.

CAM of the Month

Lang, EV, K. S. Berbaum, S. G. Pauker, et al. **Beneficial Effects of Hypnosis and Adverse Effects of Empathic Attention during Percutaneous Tumor Treatment: When being Nice does Not Suffice.** *Journal of Vascular and Interventional Radiology.* 2008 Jun; 19(6): 897-905. **Purpose:** To determine how hypnosis and empathic attention during percutaneous tumor treatments affect pain, anxiety, drug use, and adverse events. **Materials and Methods:** For their tumor embolization or radiofrequency ablation, 201 patients were randomized to receive standard care, empathic attention with defined behaviors displayed by an additional provider, or self-hypnotic relaxation including the defined empathic attention behaviors. All had local anesthesia and access to intravenous medication. Main outcome measures were pain and anxiety assessed every 15 minutes by patient self-report, medication use (with 50 mg fentanyl or 1 mg midazolam counted as one unit), and adverse events, defined as occurrences requiring extra medical attention, including systolic blood pressure fluctuations (≥ 50 mm Hg change to >180 mm Hg or <105 mm Hg), vasovagal episodes, cardiac events, and respiratory impairment. **Results:** Patients treated with hypnosis experienced significantly less pain and anxiety than those in the standard care and empathy groups at several time intervals and received significantly fewer median drug units (mean, 2.0; interquartile range [IQR], 1-4) than patients in the standard (mean, 3.0; IQR, 1.5-5.0; $P = .0147$) and empathy groups (mean, 3.50; IQR, 2.0-5.9; $P = .0026$). Thirty-one of 65 patients (48%) in the empathy group had adverse events, which was significantly more than in the hypnosis group (eight of 66; 12%; $P = .0001$) and standard care group (18 of 70; 26%; $P = .0118$). **Conclusions:** Procedural hypnosis including empathic attention reduces pain, anxiety, and medication use. Conversely, empathic approaches without hypnosis that provide an external focus of attention and do not enhance patients' self-coping can result in more adverse events. These findings should have major implications in the education of procedural personnel. copyright 2008 SIR.

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