Review of the International Research Conference on Food, Nutrition, and Cancer, 2004

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More than 400 attendees from 24 different countries attended the International Research Conference on Food, Nutrition, and Cancer sponsored by the American Institute for Cancer Research/World Cancer Research Fund International (AICR/WCRF), held July 15–16, 2004, in Washington DC. This was the third annual AICR/WCRF international research conference on this topic. The delegates included 75 international registrants and 74 dietitians. Marilyn Gentry, president of AICR and WCRF, opened the conference. This year’s event included plenary sessions, split sessions, and 91 poster presentations that addressed a wide range of topics encompassing different disciplines of ongoing global diet-cancer research. A progress update on the preparation of the second WCRF/AICR Expert Report Food, Nutrition, Physical Activity and the Prevention of Cancer: A Global Perspective was given during the conference luncheon. The evidence linking food, nutrition, and physical activity to the risk of developing cancer will be obtained from 17 systematic literature reviews (SLR) of >20 cancer sites and one literature review of cancer survivors. During 2003, the novel methodology developed for formulating the SLRs was successfully assessed for its feasibility, utility, and reproducibility. Substantive SLRs were started in January 2004.

As global obesity continues to reach epidemic proportions and concern grows about the link between obesity and cancer risk, the variables calorie intake and physical activity in the overall energy balance equation are being increasingly studied in cancer prevention research. A major focus of the conference was the current status of different types of research in this area, including both epidemiological studies and mechanistic studies—to the level of genetic interactions. For many years calorie restriction (CR) has been known to retard the aging process in laboratory rodents and to oppose the development of diverse age-associated biological changes and diseases, including several different types of cancer. The keynote address provided an overview of progress in identifying underlying mechanisms of actions of CRs in preventing aging, including ongoing research in nonhuman primates. Even though aging studies in humans are in relative infancy, it is already known that 60% of all newly diagnosed malignant tumors and 70% of all cancer deaths occur in persons aged 65 and older. Human health studies have linked higher calorie intakes to increased risk of developing prostate, breast, gastrointestinal tract, and brain cancer. Future research should disentangle the interrelationships among aging, calorie intake, and human cancer as we focus our interest on the possibility that the health benefits of CR seen in rodents may occur in people.

The conference’s first plenary session began with a lecture on calorie intake and cancer prevention as investigated by diet–gene interaction studies in genetically engineered mouse models. The use of these models established that pathways dependent on insulin-like growth factor (IGF)-1 are affected by CR, which may be one of the mechanisms involved in the anticancer effects of CR. Another presentation discussed the results on breast cancer risk factors and breast cancer occurrence drawn from the DOM cohorts among women exposed to the Dutch famine of 1944–1945. Opposing effects were found on the breast cancer risk factors of shortening of leg length, later menarche, and earlier menopause, whereas the risk biomarkers urinary estrogens and plasma IGF-1 and IGF-binding protein-3 were increased, as was breast cancer itself. Discussion of the overall results provided a warning that, in humans, relative short periods of CR can affect breast cancer risk in unexpected and opposing directions, depending on the reproductive developmental stage when exposed. The effects of obesity and increased physical activity on physiological and biological factors that have been associated with breast cancer risk were discussed for pre- and postmenopausal women in a subsequent presentation in this session. Another speaker addressed the problem of whether preventing weight gain by CR, increased physical activity, or their combination has comparable effects on the risk for breast cancer. These effects may result from changes in energy balance.

An afternoon split session covered the current status of...
knowledge concerning the role of dietary (n-3) and (n-6) fatty acids in cancer prevention and treatment. The (n-3) fatty acids eicosapentaenoic acid and docosahexaenoic acid have been shown to inhibit the proliferation of breast and prostate cell lines in vitro and to reduce the risk and progression of these tumors in animal models. However, as discussed by the first speaker in this session, the data from epidemiological studies does not consistently support these findings. Most studies have not shown an association between fish consumption or marine fatty acid intake and risk of hormone-related cancers. Another presentation was of new, compelling evidence that, in a mouse model, dietary stearidonic, eicosapentaenoic, and docosahexaenoic acids inhibit intestinal tumorigenesis by antagonizing arachidonic acid metabolism. Evidence that the chemopreventive effects of (n-3) fatty acids on colon cancer are mediated by cyclooxygenase-dependent and cyclooxygenase-independent pathways was the subject of another presentation. Identifying the target molecules and further understanding the mechanisms of these chemopreventive effects by (n-3) fatty acids can potentially lead to the development of more effective chemopreventive regimes and better dietary management of patients with colon cancer. The fourth presentation discussed the potential efficacy of (n-3) fatty acids used in combination with standard therapies to improve cancer treatment outcomes and to suppress cachexia and improve quality of life in cancer patients. The final speaker presented supporting evidence for a role of lipid peroxidation reactions and proinflammatory compounds in tumorogenesis and cachexia. Some evidence that the anti-inflammatory (n-3) fatty acids and positional isomers of the (n-6) fatty acid linoleic acid slow tumor growth and prevent cachexia was also presented. This speaker concluded that evidence is not sufficient for making dietary recommendations about fatty acid intake.

The first of 2 split sessions on phytochemicals began with a presentation on polyphenol metabolism and availability that emphasized that clearly observed in vitro effects are often not relevant to their in vivo action; dietary levels of a compound are not equivalent to what becomes available at the target site. Overall, more clinical studies on polyphenols are needed before the extent by which these compounds affect cancer risk can be conclusively assessed. The second lecture slot was filled by two presentations of new research concerning the identification and the mode of action of specific polyphenols (sirtuin activators) that extend life span in model organisms and the mimicking of CR by resveratrol at the level of gene activation. In another presentation, the speaker discussed how chlorophyllin acts as an antimutagen and anticarcinogen against aflatoxin B1 and the heterocyclic amines from grilled meat. Paradoxically, this compound was shown to increase the incidence of colon tumors in rats, although promotion was highly dose dependent, and high levels of chlorophyllin stimulated apoptosis of cancer cells in the rat gastrointestinal tract and in human colon cancer cells. The fourth presentation in this session concerned the synergistic interaction between grape seed extract and a specific rodent diet in chemoprevention in the dimethylbenzyl[a]anthracene rat mammary tumor model. Finally, the molecular mechanisms by which the green tea catechin, epigallocatechin gallate, inhibits tumor angiogenesis in animal models were discussed.

The second split session on phytochemicals emphasized multiple modes of action and synergistic interactions. The initial presentation began with the challenging question of why single antioxidants, e.g., β-carotene, often have effects on cancer prevention that are opposite to their effects when given in combination with other antioxidants. Doses and combinations of additive and synergistic actions are important considerations with regard to the antioxidant and antiproliferative effects of phytochemicals, emphasizing the importance of whole fruit and vegetable consumption in the human diet. The second presentation further emphasized this recommendation in a comparison of the reduction of prostate tumor incidence in rats fed either isolated lycopene or tomato powder. The latter was more effective than lycopene alone. Furthermore, in a rat Dunning tumor model, broccoli powder plus tomato powder had the greatest effect in reducing tumor growth, supporting the AICR recommendation of a diet rich in different kinds of vegetables for cancer prevention. The third speaker presented his research on indole-3-carbinol and prostate cancer. This compound, found in cruciferous vegetables, inactivates nuclear factor-κB and Akt signaling pathways, and induces prostate cancer cell apoptosis. These features, combined with indole-3-carbinol’s regulation of genes related to the control of cell proliferation, cell cycle, and oncogenesis, and its role in the detoxification of carcinogens indicate the potential of indole-3-carbinol as an agent both in the prevention and the treatment of prostate cancer. A fourth researcher discussed his findings with aqueous extracts of broccoli seeds containing glucosinolates in the chemoprotective response in mouse organs and rodent liver cell lines. Collectively, the results showed that these extracts are effective at inducing antioxidant proteins and detoxification enzymes, including glutathione transferases in an Nrf2-dependent manner. The final presentation in this session described how nutritional antioxidants could modulate the effects of reactive oxygen and nitrogen species on gene expression. Importantly, selenium supplementation of the diet in human subjects was shown to increase the selenium content of selective body proteins.

During the morning of the second day of the conference, a split session focused on the potential roles of vitamins A, D, and E in cancer prevention and treatment. One presentation discussed how vitamin A deficiency can result in an impairment of the function of the respiratory epithelium. In heavy smokers, a similar impairment, possibly involving a localized deficiency of vitamin A caused by an interference with vitamin A metabolism, may promote the development of lung cancer. Topical application of retinol esters may be a promising therapy for local retinol deficiencies and consequential morphological alterations in the epithelium. The second presentation discussed new findings, showing that aberrant vitamin A metabolism may be associated with invasive bladder cancer. The third presentation described how ongoing studies are showing that certain vitamin E derivatives and analogues induce a wide variety of epithelial cancer cells, but not normal cells, to undergo apoptosis in cell culture. Some success in reducing tumor cell burden and metastasis in a mouse mammary cancer model by synthetic vitamin E and an α-tocopherol ether-linked acetic acid analogue has also been achieved. This analogue deserves evaluation as part of chemotherapeutic treatment of primary tumors as well as for prevention of recurrence by reducing metastasis. The next presentations focused on vitamin D and colon carcinogenesis and skin cancer, respectively; both studies outlined the complexities of vitamin D metabolism in the body and its interactions with calcium. Nonhypercalcemic analogues of the active form of vitamin D3 [1α,25(OH)2D3] may have effective chemopreventive properties against intestinal carcinogenesis. Keratinocytes can convert vitamin D to 1α,25(OH)2D3, which stimulates their differentiation in interactions with calcium, raising the hope that this compound can prevent the development of malignancies. However, this tight regulation of
differentiation breaks down in squamous-cell carcinomas, as has been detailed by mechanistic studies.

The final plenary session of the conference included evidence-based investigations of cancer prevention and cancer survivorship. The first presentation discussed study aims, design, and progress in the European Prospective Investigation into Cancer and Nutrition (EPIC). This study is examining dietary patterns as well as specific nutrients that protect against cancer end points. An inverse association between dietary fiber and colorectal cancer was found; in some cohort studies, high saturated fat intake was associated with breast cancer risk, and high fruit and vegetable intake was inversely associated with cancer mortality. Recent results from EPIC showed that isoflavones and lignans slightly increase the risk for breast cancer in contrast to results from earlier epidemiological and experimental studies. The authors of the EPIC study emphasize that the earlier studies were done on Asian populations and may have resulted from premenopausal effects. The second speaker discussed several ongoing National Cancer Institute clinical trials in nutrients and cancer prevention end points. Breast cancer prevention clinical trials include bioactive food components: indole-3-carbinol, sulforaphane, isoflavones, perillyl alcohol, and green tea polyphenols. Studies have been designed to include assessment of data from nonhormonal pathways related to breast cancer occurrence. Prostate cancer prevention trials with the potentially bioactive food compounds selenium, vitamin E, soy isoflavones, and green tea polyphenols are also underway. The results of these studies will be complemented by nutrigenomic approaches to study diet-cancer interactions.

AICR and WCRF are also concerned with nutritional and physical activity support for cancer survivors both during and after treatment. Recommendations for cancer survivors may differ from those for primary cancer prevention and will require investigation by different experimental approaches, including intervention trials. An SLR of randomized controlled trials designed to investigate whether diet or physical activity affects cancer survival was conducted at the University of Bristol, UK. This endeavor clearly showed the paucity of studies relating these interventions to mortality, recurrence, and quality-of-life end points for cancer survivors. Overall, the results were inconclusive or negative with regard to basing diet and physical fitness recommendations for cancer survivors on those recommended by AICR for cancer prevention. The effects of interventions could not be estimated from the few trials, and all reported findings—including those that a generic healthy diet encompassing reduced calorie intake and increased fiber, fruit, and vegetable intake might reduce all-cause mortality—were also compatible with no effect. Data were too sparse for conclusions to be drawn about cancer specific mortality and cancer recurrence. Clearly, there is a tremendous need for new research with all available experimental approaches, including large-scale clinical trials and evidence-based medicine.

In their landmark publication in 1997, AICR and WCRF issued 14 recommendations regarding diet and lifestyle factors designed to reduce cancer incidence and mortality on a global basis. At this year's research conference, the results of a recently published study on morbidity and mortality in the Iowa Women's Health Study cohort after differential adherence to these recommendations were presented by one of the study's coauthors. Study participants were assessed for subsequent cancer incidence and mortality after following up to 9 of these recommendations. The overall data support that adherence to the AICR/WCRF recommendations, independently and in conjunction with not smoking, is likely to have a substantial public health impact on reducing cancer incidence and, to a lesser degree, cancer mortality at the population level.

The final lecture of the conference covered evidence-based overviews of cancer prevention and their derived dietary and lifestyle guidelines, including those of AICR and WCRF. The complete sequencing of the human genome and steadily advancing nutrigenomic techniques have evoked a change in medical practice where evidence- and population-based protocols together open the door to the provision of personalized nutrition recommendations and specialized medical treatment. This concluding lecture offered an exciting challenge to cancer researchers in the fields of nutrition, obesity, and physical activity—to conduct studies from all angles and designs, including genomic medicine, to approach the development of protocols for cancer prevention and treatment.

AICR is a member of the WCRF global network, which provides a wide range of education programs to help people make changes for lower cancer risk and supports innovative research in prevention and treatment worldwide.