Nutrition and cancer: the current epidemiological evidence

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We have examined the current scientific evidence on the relationship between nutrition and the most frequent tumours in the Spanish population: lung, colorectal, prostate, breast and stomach. Consumption of fruit is negatively associated with cancer of the lung and stomach, possibly with colorectal cancer, but probably not with prostate cancer and breast cancer. Consumption of vegetables probably reduces the risk of colorectal and stomach cancer, but probably is not associated with cancer of the lung, prostate and breast. Consumption of red and processed meat is positively associated with colorectal cancer and probably with stomach cancer. Animal fat is possibly associated with colorectal cancer and probably with prostate and breast cancer. High alcohol intake increases the risk of colorectal and breast cancer, while dairy products and calcium seem to decrease the risk of colorectal cancer. Obesity is a recognised risk factor of colorectal cancer and breast cancer in postmenopausal women, while foods with a high glycaemic index and glycaemic load possibly increase the risk of colorectal and prostate cancer. The relevance of nutrition on the cancer process is evident. Nevertheless important issues remain to be solved and further studies are needed. This accumulative knowledge should be used by public health authorities to develop recommendations and activities to reduce overweight and obesity and to promote healthy dietary habits.

Nutrition and cancer: Epidemiological evidence

It is widely accepted that nutrition has an important role in cancer occurrence, being the most important cause of cancer after smoking. In 1997, an important report from an international expert committee (World Cancer Research Fund/ American Institute for Cancer Research, 1997; hereafter referred to as the WCRF/AICR report) summarised the scientific evidence on the effect of food and nutrients up to the middle of the last decade. It was estimated that between 30 and 40 % of cancer incidence worldwide was preventable by healthy eating, weight control and appropriate physical activity. However, at the time of publication of this report, the evidence was considered convincing in a limited number of associations: a high intake of vegetables and fruit decrease the risk of oropharynx, oesophagus, lung, stomach and colorectal cancer; physical activity is associated with colon cancer; use of refrigeration decreases stomach cancer; and alcohol consumption is causally associated with cancer of the oropharynx, larynx, oesophagus and liver.

Further evidence has been published in the last 8 years. In the present article, we describe the most recent findings related to the most frequent cancers in our society: lung, colon and rectum, prostate, breast and gastric. Fibre as a protective factor in colorectal cancer is described in an accompanying article.

Food, nutrition and lung cancer

Lung cancer is the most frequent tumour in males (22.2 % of cancer incidence) and the seventh in females (3.5 % of cancer incidence) in the Spanish population. Up to 1997 (WCRF/ AICR report), it was considered that there was convincing evidence that diets high in vegetables and fruit (particularly green vegetables and carrots) protect against lung cancer. This conclusion was based on seven cohort studies and seventeen case-control studies. On the other hand, it was considered that probably carotenoid intake and possibly vitamin C, vitamin E and Se intake protect against lung cancer, while animal fat possibly increases the risk.

Thereafter, a pooled analysis of eight cohort studies (Smith-Warner et al. 2003) was published in which a protective effect of fruit (relative risk (RR) = 0.77; 95 % CI 0.67, 0.87) was observed with a dose-response relationship (P<0.001), but the effect was weaker for vegetables (RR = 0.88; 95 % CI 0.78, 1.0) and without dose-response. The authors concluded that there was a modest reduction in the lung cancer risk, mostly attributable to fruit, but not to vegetable intake. A recent meta-analysis (Riboli & Norat, 2003) found a significant but slight protective effect of fruit and vegetables in case-control studies; however, in cohort studies the protective effect was observed to be associated with fruit intake (odds ratio (OR) = 0.86; 95 % CI 0.78, 0.94), but not associated with vegetable intake. Other pooled analysis focused on nutrients (Mannisto et al. 2004) observed a protective effect only of β-cryptoxanthin (RR = 0.76; 95 % CI 0.67, 0.86), but not in relation to other carotenoids. Finally, the results from European Prospective

Abbreviations: AICR, American Institute for Cancer Research; EPIC, European Prospective Investigation into Cancer and Nutrition; OR, odds ratio; RR, relative risk; WCRF, World Cancer Research Fund.

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Investigation into Cancer and Nutrition (EPIC; Miller et al. 2004), the largest cohort study in the world, showed a significant inverse association between fruit consumption and lung cancer (RR for the highest quintile of consumption relative to the lowest = 0·60; 95 % CI 0·46, 0·78). However, there was no association between vegetable or vegetable subtype consumption and lung cancer. Overall, in relation to nutrition and lung cancer this recent evidence confirms the protective effect of fruit but not of vegetables (Table 1).

Regarding the intake of animal fat and the possible increase of risk of lung cancer, a recently published pooled analysis of eight cohort studies (Smith-Warner et al. 2002) did not support an association between fat or cholesterol intake and lung cancer risk.

**Food, nutrition and colorectal cancer**

Colorectal cancer is the second most frequent tumour in males and females in the Spanish population, representing 14·1 and 17·2 % of the total cancer incidence, respectively. Up to 1997 it was stated (WCRF/AICR report) that there was convincing evidence that a high intake of vegetables and regular physical activity decrease the risk of colorectal cancer; that probably alcohol and red meat increase the risk, that possibly a high intake of fibre decreases the risk and that obesity increases the risk. It was also concluded that possibly Ca intake has no relationship with colorectal cancer.

Over the last year, further evidence has confirmed that high intake of red and processed meat is positively associated with the risk of colorectal cancer. A pooled analysis on thirteen cohort studies on meat consumption and colorectal cancer (Sandhu et al. 2001) has shown a 12–17 % increase risk of colorectal cancer for each daily increase of 100 g red meat, and a 49 % increase of risk for each daily increase of 25 g processed meat. Furthermore, a comprehensive review of all epidemiological studies published between 1973 and 1999 (Norat et al. 2002) concluded that for each daily increase of 120 g red meat intake the risk of colorectal cancer increased 24 %, and the risk is increased 36 % for each daily increase of 30 g in consumption of processed meat.

A recent publication has also confirmed the positive association between alcohol intake and colorectal cancer. A pooled analysis of eight cohort studies (Cho et al. 2004) has shown that an alcohol intake greater than 45 g/d (approximately more than three drinks a day) is associated with a 41 % increase of colorectal cancer risk (RR = 1·41; 95 % CI 1·16, 1·72).

However, in relation to fruit and vegetables, a recent meta-analysis (Riboli & Norat, 2003) showed a significant but slight protective effect of vegetable intake (OR = 0·87; 95 % CI 0·80, 0·95) and fruit intake (OR = 0·93; 95 % CI 0·87, 0·99) in case–control studies, but no association in cohort studies.

Recent epidemiological studies have given rise to new hypotheses about the potential role of elevated level of insulin-like growth factors and other related factors in the pathogenesis of colorectal cancer. This is part of a complex metabolic syndrome, characterised by general obesity and intra-abdominal body fat, physical inactivity, hyperinsulinaemia and alteration in the metabolism of endogenous hormones (oestrogens, androgens, insulin-like growth factors and their binding proteins) that could be associated with the risk of colorectal cancer but also to prostate, pancreas and breast cancer (Kaaks & Lukanova, 2001). A diet with a high content of glycaemic index and glycaemic load could be an important component of this metabolic syndrome.

With regard to dairy products, most recent evidence showed a moderate protective effect of total dairy products, milk and Ca on the risk of colorectal cancer. A recent review (Riboli & Norat, 2003) concluded there was a moderate protective effect for total dairy products and milk in cohort studies, although this was not observed in case–control studies. A pooled analysis of ten cohort studies (Cho et al. 2004) showed that milk consumption of more than 250 g/d in comparison with less than 10 g/d is associated with a 15 % reduction of the risk of colorectal cancer. The highest v. the lowest dietary intake of Ca was associated with a 14 % reduction of risk. A 22 % of reduction was observed when dietary and supplement intake were considered simultaneously. A Cochrane review has been published (Weingarten et al. 2004) about the effect of Ca supplementation. A moderate protection in two randomised controlled trials on the development of adenomatous polyps of the colon was observed. However, it was concluded that there was insufficient evidence to recommend the general use of Ca supplementation for the prevention of colorectal cancer.

**Food, nutrition and prostate cancer**

Prostate cancer is the third most frequent cancer in men in Spain. About 12·7 % of cancer cases in the male Spanish population are

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**Table 1. Groups of foods associated with selected cancers according to current epidemiological evidence**

<table>
<thead>
<tr>
<th>Foods</th>
<th>Lung</th>
<th>Colorectal</th>
<th>Prostate</th>
<th>Stomach</th>
<th>Breast</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total fruit</td>
<td>(−)</td>
<td>S/Pr</td>
<td>(−)</td>
<td>(−)</td>
<td>Pr</td>
</tr>
<tr>
<td>Total vegetables</td>
<td>(NA)</td>
<td>Ps</td>
<td>(−)</td>
<td>Pr</td>
<td>(−)</td>
</tr>
<tr>
<td>Red and processed meat</td>
<td>(+)</td>
<td>(−) Ps</td>
<td>(−)</td>
<td>(−) Pr/Ps</td>
<td>(−) Ps</td>
</tr>
<tr>
<td>Animal fat</td>
<td>(NA)</td>
<td>Ps</td>
<td>(+)</td>
<td>(+) Pr/Ps</td>
<td>(+) P</td>
</tr>
<tr>
<td>Salted food</td>
<td>(NA)</td>
<td>Pr</td>
<td>(+)</td>
<td>(−) S/Ps</td>
<td>(+) S/Ps</td>
</tr>
<tr>
<td>Alcohol</td>
<td>(NA)</td>
<td>Pr</td>
<td>(+)</td>
<td>(−) S/Ps</td>
<td>(+) S/Ps</td>
</tr>
<tr>
<td>Food with high glycaemic load</td>
<td>(+)</td>
<td>Pr</td>
<td>(+)</td>
<td>(−) P</td>
<td>(+) S/Ps</td>
</tr>
<tr>
<td>Dairy products</td>
<td>(+)</td>
<td>Pr</td>
<td>(−)</td>
<td>(−) S</td>
<td>(NA) P</td>
</tr>
<tr>
<td>Obesity</td>
<td>(+)</td>
<td>S</td>
<td>(NA) P</td>
<td></td>
<td>(−) S</td>
</tr>
</tbody>
</table>

Association: −, negative; +, positive; NA, no association. Level of evidence: S, sufficient; Pr, probable; Ps, possible.

*According to the evaluation of the current epidemiological evidence done by the author.*
Food, nutrition and breast cancer

Breast cancer is the most frequent cancer in women in Spain. More than 28% of cancer cases in women are breast cancer. The 1997 WCRF/AICR report concluded that saturated fat, meat and breast cancer has become very controversial. In contrast, a recent pooled analysis of eight cohort studies showed no evidence of a protective effect of fruits and vegetables (Smith-Warner et al. 2001). Another meta-analysis (Riboli & Norat, 2003) found a slight protective effect in fifteen case-control studies, while found no relationship in the analysis of ten cohort studies. Finally, the EPIC study did not show any relationship with vegetable and fruit intake (van Gils et al. 2005).

Recent publication of a collaborative reanalysis of fifty-three epidemiological studies (Hamajima et al. 2002) has confirmed that alcohol is causally associated with breast cancer. An increase of 10 g alcohol per day is associated with an increased risk of breast cancer, while probably alcohol and possibly saturated and animal fat increase the risk. In contrast, a recent pooled analysis of eight cohort studies showed no evidence of a protective effect of fruits and vegetables (Smith-Warner et al. 2001). Another meta-analysis (Riboli & Norat, 2003) found a slight protective effect in fifteen case-control studies, while found no relationship in the analysis of ten cohort studies. Finally, the EPIC study did not show any relationship with vegetable and fruit intake (van Gils et al. 2005).

Food, nutrition and gastric cancer

Gastric cancer is the fifth most frequent cancer in the Spanish population. About 61% of cancer incidence in men and 55% of cancer incidence in women are gastric cancers. In 1997, the WCRF/AICR report concluded that there was no evidence of a convincing or probable causal relationship with diet. It was stated that vegetable intake may decrease the risk of prostate cancer and that animal fat, animal protein and red meat may increase the risk. Since then, results from the EPIC cohort study on prostate cancer incidence and the consumption of vegetables and fruit have been published (Key et al. 2004). No significant association between total vegetables, cruciferous vegetables, total fruit, and total fruit and total vegetables combined was observed. The finding of a possible protective effect of lycopene remains to be confirmed. The relevance of nutrition on the cancer process is evident. Even so, despite the large number of epidemiological studies carried out up to the present, the evidence about the effect of some important foods and groups of food is limited and some results are still inconsistent. Important issues remain to be solved and further studies are needed. However, the relationship between nutrition and cancer is more complex than it was previously considered to be. In order for scientific knowledge to be useful, it is necessary to have a better understanding of the role of foods in the etiology of cancer.

Conclusion

We have examined the cumulative scientific evidence on the relationship between nutrition and the most frequent cancers. The relevance of nutrition on the cancer process is evident. Even so, despite the large number of epidemiological studies carried out up to the present, the evidence about the effect of some important foods and groups of food is limited and some results are still inconsistent. Important issues remain to be solved and further studies are needed. However, the relationship between nutrition and cancer is more complex than it was previously considered to be. In order for scientific knowledge to be useful, it is necessary to have a better understanding of the role of foods in the etiology of cancer.
be improved, it is necessary to study results from large prospective studies, carried out in populations with heterogeneous dietary habits, reducing the level of measurement errors and using multidisciplinary approaches including biochemical markers, molecular biology and genetic markers.

Finally, this cumulative knowledge should be used by public health authorities to promote nutritional recommendations for better and healthier nutrition. In Spain, it is imperative to develop public health measures to reduce overweight and obesity and to promote healthy dietary habits.

References


