32

Nutrition and cancer

Mark L. Wahlqvist and Antigone Kouris-Blazos

OBJECTIVES

- To understand how nutritional factors may contribute to the development of cancer.
- To consider whether nutritional prevention of cancer is feasible.
- To briefly review the role of diet in helping those with cancer.

INTRODUCTION

Following cardiovascular disease, cancer is the second leading cause of death in most developed countries; about one in three persons will be diagnosed with cancer during their lifetime, and about 60% of those diagnosed will die of cancer (see Chapter 40). It is likely that cancer will become the leading cause of death if cardiovascular death rates continue to decline. In developed countries cancers of the lung, colon, breast and prostate contribute most to incidence and mortality. In poorer regions, cancers of the stomach, liver, oral cavity, oesophagus and uterine cervix are more common. However, many developing countries are experiencing a transition from the cancer incidence patterns of poorer to those of affluent areas. Breast cancer rates have been increasing in almost all countries (Willet 1999).

CANCER, GENES AND LIFESTYLE

There is a kind of fatalistic approach to genes that many people seem to have now—that if your parents, sister or brother had something, you are doomed to have it too. Even though there are genes that cause high

rates of cancer in some families, such fatalism, for the most part, is not warranted. New research in the cancer field indicates that genetics may not play as large a role in cancer risk as once thought. In fact, environmental factors may be a more important contributor to cancer risk than previously thought. Lichtenstein et al. (2000) conducted a study of 44 788 twins in Finland, Denmark and Sweden to assess cancer risk for breast, colorectal, prostate, stomach and lung. Overall, genetic factors seemed to account for between 21 and 42 per cent of cancer risk, depending on the type of cancer, with an average of about 30 per cent. This study estimated the genetic risk of developing prostate cancer at 42 per cent, colorectal cancer at 35 per cent and breast cancer at 27 per cent. However, these were estimates only and the risks could be much lower. The rest of the cancer risk was due to environmental factors—a broad category including experiences in the womb, upbringing, occupation and lifestyle. Most types of cancer showed little impact of shared genes. Rates of concordance were generally higher in monozygotic twins than dizygotic twins, but even for genetically identical twins there was a less than 15% chance of developing the same cancer. This study does not take into account specific types and degrees of exposure to environmental risks, such as tobacco use or diet, thus issues of gene and environment interaction were not fully explored. Despite its limitations, this study provides new and valuable information for the nature versus nurture debate. It reinforces evidence that genetics play a significant role in susceptibility, but that most cancers are caused by carcinogens such as tobacco, diet and bacteria or viruses. Due to the influence of environment on cancer risk, diet can either reduce or exacerbate a genetic predisposition.

WHAT IS CANCER?

Cancer is the term used to refer to a variety of uncontrolled tissue proliferations. Cancers might otherwise be termed *tumours* of the malignant kind as opposed to benign; the difference is one of propensity to spread. Neoplasia or neoplastic disease are less emotive terms than cancer to describe disorders of tissue proliferation.

Division of cells, or cell multiplication, is a normal event that allows tissue development or regeneration. It is when the factors controlling the cell's division or its expected death (apoptosis) are no longer operative that neoplastic disease occurs. It is probably normal for aberrant cells to be produced occasionally. This might be because a genetic mutation has occurred. Mutations can result from exposure to certain chemicals, radiation or viruses. If there are not too many aberrant cells, the body's defence system can probably get rid of them. Theoretically, nutritional factors could influence neoplastic disease development (oncogenesis) by affecting mutation, by regulation of cell death or through the defence system.

STEPS IN CARCINOGENESIS AND HOW NUTRITION MAY INFLUENCE THEM

Carcinogenesis refers to the steps by which a cancer may develop, shown in Table 32.1.

What we eat may play a role for each of the steps of carcinogenesis. Food may contain mutagens, like aflatoxins produced by moulds, or nitrosamines produced from food nitrites, or nitrates (present naturally and added to food), and so *initiate* cancer. There are a number of anti-mutagens in food which have been reviewed by Bronzett (1994). These may be bioanti-mutagens which reduce DNA damage (vanillin from the vanilla plant, cinnamaldehyde from cinnamon, and chlorophyllin related to chlorophyll) and desmutagens which inactivate mutagens (the peptide glutathione as antioxidant, vitamin E as antioxidant, vitamin C for nitrite). Food and beverage may also *promote* cancer (as with alcohol in the upper gut or airways; or impaired immune function) or *inhibit* cancer (as when immune function is stimulated, see also Chapter 31). What is eaten may encourage *progression* (by various growth

Table 32.1 Mechanisms of carcinogenesis

Stages	**I** **Initiation**	**II** **Post-initiation** Progression or differentiation and growth
Role of food/ nutrition	Yes	Yes
Mechanisms	**Altered gene regulation and expression** **Mutations induced by:** ■ genotoxic chemicals ■ tumour viruses ■ radiation	**Control of cell division and death; immune surveillance**

factors in food) or slow down growth or metastases where tumours are spread by the lymphatics or bloodstream (by food components which reduce the formation of new blood vessels, a process known as angiogenesis that is required for tumour growth, such as genistein from soy products, which is anti-angiogenic) (Fotsis 1993). Apoptosis as a mechanism for inhibiting tumour growth may also be achieved by a food flavonoid known as quercetin, although it is not well absorbed and its action may be mainly within the bowel (Wei et al. 1994).

FOOD AND CANCER INCIDENCE PATTERNS

Cancer incidence patterns vary in relation to *ethnicity*, which includes food culture (Table 32.2). They may have associated non-cancer chronic non-communicable disease patterns.

A more detailed examination of the diet–cancer relationship within a region or culture can be helpful (Table 32.3) (Jensen et al. 1982). In Scandinavia, the Finns (in Helsinki and rural areas) tend to have more CHD than the Danes (in Copenhagen and rural areas), but less large bowel cancer, even though the urban and rural dietary fibre and fat intakes are comparable. But the source of fat in Finland is relatively greater from dairy products than in Denmark, and they may be protective against large bowel cancer on account of the effects of the non-fat components of dairy products, like whey protein or calcium (or vitamin D where this is added to milk). Such patterns are not immutable; they often change with migration. Examples include the decrease in stomach (gastric) cancer and the increase in large bowel (colorectal) cancers among first-generation Japanese migrants to Hawaii and, even more markedly, to California. Likewise, Mediterranean peoples who migrate to Australia exhibit similar trends (McMichael et al. 1980) (Figures 32.1 and 32.2).

Even within cultures at a particular geographical location, changes in cancer incidence are taking place in response to lifestyle change. For example, in Australia in 1985 the annual rate of change in age-standardised cancer incidences was substantial and different, cancer by cancer (Table 32.4) (Lester and NH&MRC 1994). In much of the Asia and Pacific region, cancer incidence patterns are transitional between those which have characterised the Orient on the one hand and the Occident on the other (Table 32.2).

Table 32.2 Diet–cancer patterns with the associated non-cancer disease patterns

	Oriental	Mediterranean	Other Occidental
Cancer	gastric primary hepatic oral naso-pharyngeal oesophagus	gastric	breast colorectal pancreas endometrium ovary prostate
Non-cancer chronic non-communicable disease	CVD diabetes	obesity CHD	obesity CVD diabetes

CVD: cerebrovascular disease
CHD: coronary heart disease

Table 32.3 Large bowel cancer and diet in Scandinavia

	Finland		Denmark	
	Rural	Helsinki	Rural	Copenhagen
Incidence rate (per 10^5)				
colon cancer	6.7	17.0	12.9	22.8
colorectal cancer	14.2	25.7	27.9	42.1
Diet (g/day)				
total fibre	18.4	14.5	18.0	13.2
total fat	133	102	146	117
cereal	376	241	262	203

Source: Jensen et al. 1982

Table 32.4 Annual rate of change in age-standardised rate (ASR) of diet-related cancers in Australia in 1985

	Males		Females	
	ASR	Annual change (%)	ASR	Annual change (%)
stomach	13.1	–0.3	5.1	–3.6
colon	28.9	+5.8	23.6	+2.4
rectum, anus	16.7	+0.6	10.7	+1.0
gall bladder	1.9	–1.7	2.1	+1.0
female breast	–	–	59.2	+2.1
uterus	–	–	10.0	+10.7

ASR is standardised to the World Standard Population. The average annual incidence is expressed per 100 000 over the period 1982–85.

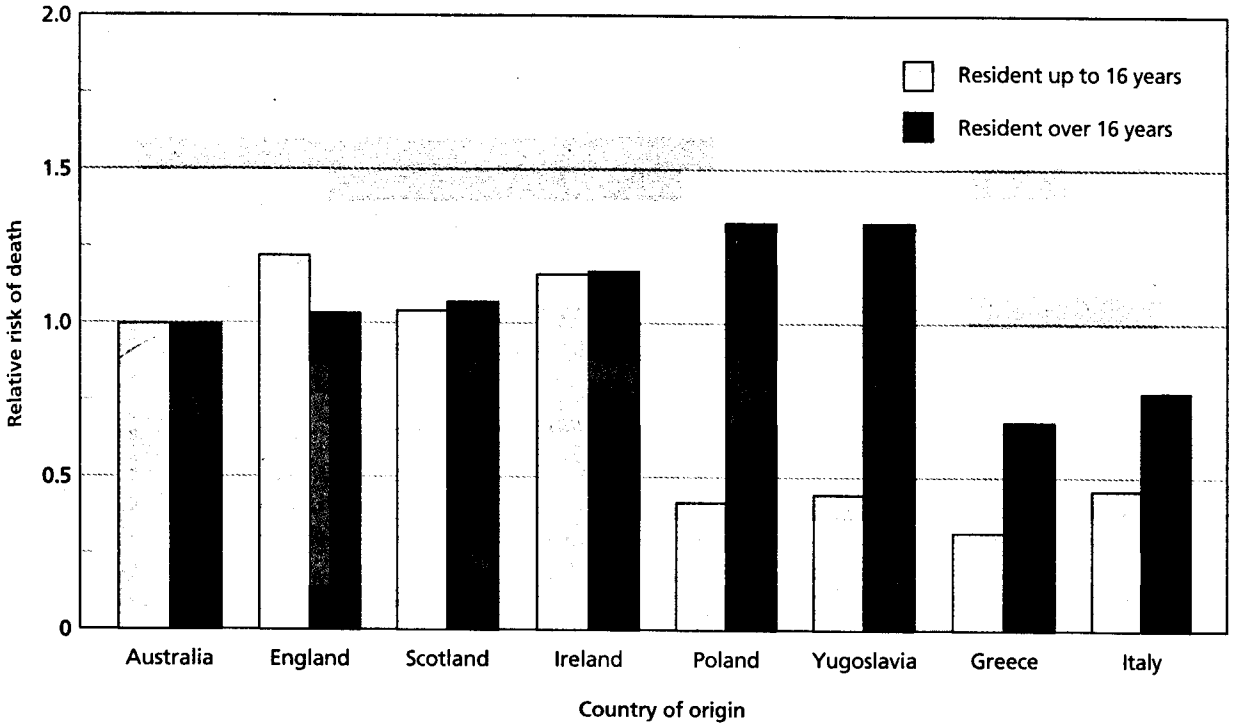

Figure 32.1 Age–sex standardised relative risk of death by length of residence in Australia: rectal cancer

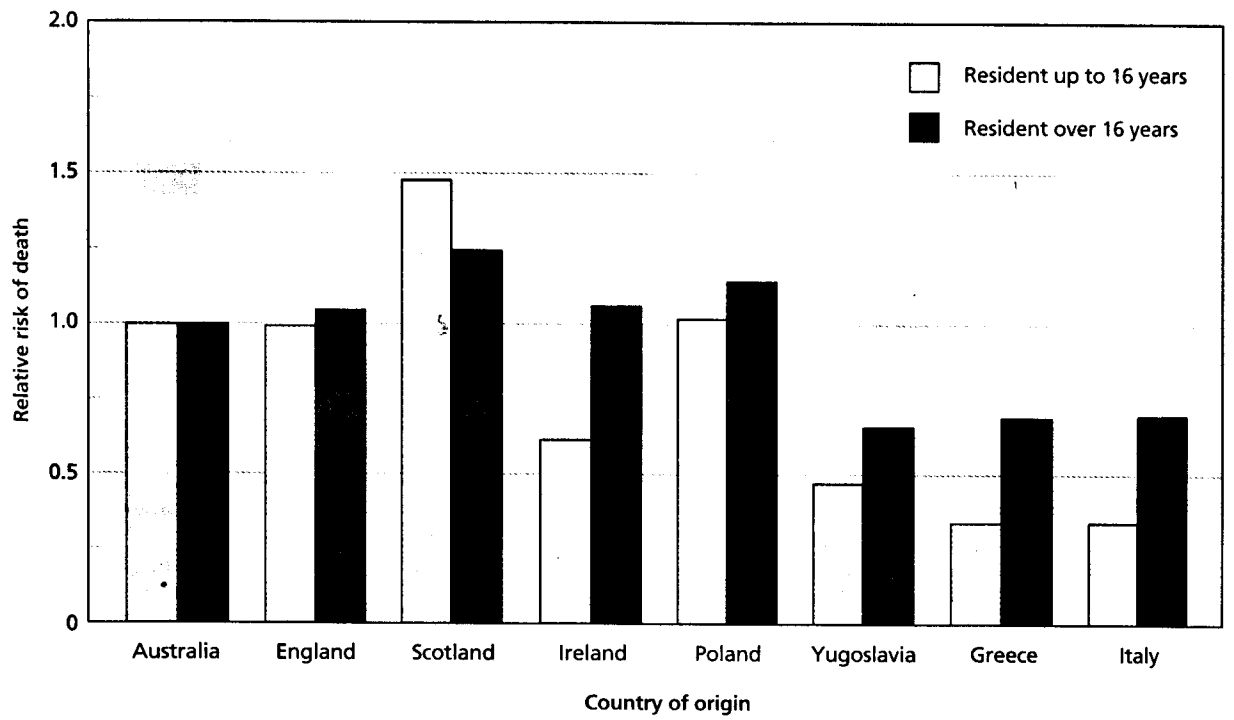

Figure 32.2 Age–sex standardised relative risk of death by length of residence in Australia: colon cancer (McMichael et al. 1980)

NUTRITIONAL RISK FACTORS FOR CERTAIN CANCERS

The mechanisms by which food and food components influence the development of cancer still often lack detailed understanding (Table 32.1). But it is becoming clear that a number of factors in food, not only those which are described as nutrients, are important. For example, all of those factors which alter immune status may, in turn, affect the risk of cancer (Chapter 31). The immunodeficiency associated with ageing, with HIV-positivity, and with transplantation of organs where immunosuppression is required, increases the risk of cancer.

Examples of nutritional risk factors for certain cancers are given in Table 32.5.

The case for these risk factors is derived from several lines of evidence. These may be experimental in animals; cross-sectional in human populations (where food–health relationships are examined); case-control in humans where the differences in food intake between those who have and do not have a cancer type are analysed; observational in humans over extended periods of time (the Melbourne Cohort Study of 41 500 individuals of different ethnic background for 25 years is an example); or intervention, where a change in food or nutrient intake is made in a controlled and randomised way and outcome for a cancer or its precursor (like bowel polyps for colon cancer) is evaluated. No one study type provides enough conclusive evidence, even with intervention studies where their situational or food cultural relevance needs to be taken into account. But as the evidence increases, so dietary change can be made with more confidence. Any changes ought also to favourably affect total health, morbidity and mortality and not just be related to cancer.

Fruits and vegetables

Over 200 case-control and prospective cohort studies have shown an inverse relationship between higher consumption of fruits and especially vegetables and a reduced risk of cancers at many sites. Convincing evidence exists for cancers of the lung, stomach and colon. For prostate cancer, inverse associations have been observed with tomato products, the primary source of the non-provitamin A carotenoid lycopene. The constituents in fruit and vegetables, responsible for the reduced cancer risks, are not known. Identification of the specific protective constituents, or combination thereof, may never be completely possible (Willet 1999).

Table 32.5 Nutritional risk factors for selected cancers—strength of evidence supporting relationship

	Convincing	Probable	Possible	Insufficient
Lung	■ Vegetables, particularly green vegetables and carrots, and fruits decrease risk	■ Carotenoids decrease risk	■ Physical activity, vitamin C, vitamin E and selenium decrease risk ■ Retinol has no relationship ■ Total fat, saturated/ animal fat, cholesterol and alcohol increase risk	
Stomach	■ Vegetables and fruits decrease risk. In particular, raw vegetables, allium vegetables and citrus fruits ■ Refrigeration decreases risk by reducing the use of salt and risk of contamination	■ Vitamin C decreases risk ■ Alcohol, coffee, black tea and nitrates (from vegetables) have no relationship ■ Salt and salting increases risk	■ Carotenoids, allium compounds, wholegrain cereals and green tea decrease risk ■ Sugar, vitamin E and retinol have no relationship ■ Starch, grilled/ charred/barbequed meat and fish increase risk	■ Fibre, selenium, sesame oil, onion, garlic decrease risk ■ Cured/smoked meats, *N*-nitrosamines increase risk ■ Factors encouraging certain gastric microflora, like *Helicobacter pylori*, which may lead to atrophic gastritis

Table 32.5 cont.

	Convincing	Probable	Possible	Insufficient
Bowel	■ Physical activity decreases the risk of colon cancer ■ Vegetables decrease risk (not fruits)	■ Non-starch polysaccharides decrease risk ■ Fibre, unless associated with low fat intake, increases risk ■ Alcohol, as beer, increases risk ■ Salicylates, aspirin garlic and indoles decrease risk	■ Starch, fish, carotenoids, decrease risk ■ High body mass increases the risk of colon cancer ■ Greater adult height, frequent eating, sugar, total fat, saturated/ animal fat, processed meat, eggs and heavily cooked/ barbequed meat increase risk	■ Resistant starch, vitamin C, vitamin D, calcium, whey proteins from dairy products, *Lactobacillus Bifidus* in fermented foods, vitamin E, folate, omega-3 fatty acids, methionine, wholegrain cereals and coffee decrease risk ■ Iron and omega-6 linoleic acid increases risk
Pancreas			■ Energy intake, dietary cholesterol, trypsin inhibition, larger build and high protein/fat diet may increase risk	
Prostate		■ Total fat, saturated/ animal fat may increase risk ■ Lycopene (e.g. tomatoes), soy/ phytoestrogens may decrease risk	■ Vegetables (green leafy and yellow), soy decrease risk ■ High body mass, alcohol, vitamin C, coffee and tea have no relationship ■ Meat, milk and dairy products increase risk	■ High energy intake, cadmium increases risk
Breast	■ Coffee has no relationship ■ Rapid growth and greater adult height increase risk	■ Vegetables (green), legumes (soy), fruits decrease risk ■ Dietary cholesterol has no relationship ■ High body mass (postmenopausal), adult weight gain increase risk ■ Breastfeeding reduces risk with longer total duration ■ Alcohol (>5 g/day) increases risk	■ Physical activity, non-starch polysaccharides/fibre and carotenoids decrease risk ■ Retinol, vitamin E, poultry and black tea have no relationship ■ Mono-unsaturated fats may decrease risk and omega-6 linoleic acid may increase risk ■ Total fat, saturated/ animal fat, meat increase risk	■ Vitamin C, vitamin A from foods, isoflavones, lignans, fish decrease risk ■ Animal protein and DDT in tissues increase risk
Cervix/ovaries			■ Vegetables and fruits, carotenoids, vitamin C and vitamin E decrease risk ■ Folate and retinol have no relationship ■ Galactose (milk) may increase risk of ovarian cancer	

Source: Adapted from World Cancer Research Fund/American Institute for Cancer Research 1997

Antioxidants

The lifestyle which may increase the risk of developing cancer appears to be one which is more sedentary, leading to over-fatness, one in which substance abuse of alcohol and tobacco is more common, and where food intake is more fatty and refined. These lifestyle factors may be quite intertwined. Lung cancer (of the bronchogenic kind, arising from the lining of the bronchi) can serve as an example. Cigarette smoking is unquestionably of paramount importance as a risk factor, but the consumption of green and yellow vegetables is relatively protective for a given level of cigarette smoking, according to the work of T. Hirayama in Japan and other workers (Hirayama 1979). From around 200 studies showing that people who have more fruit and vegetables in their diet are less likely to get cancer, researchers queried whether an above average intake of vitamins in supplement form could confer similar protection. Vitamins A, C, E and beta-carotene (the antioxidants, see Chapter 16) were considered the obvious choices to simulate the properties of fruit and vegetables, but it could well have been other nutrients or non-nutrients present in plant food. In January 1996, investigators conducting a large study of the combination of beta-carotene and vitamin A as preventive agents for lung cancer in smokers had to tell the 18 000 participants to stop taking their vitamin pills two years before the study was scheduled to finish. Interim results showed 28% more lung cancers and 17% more deaths in participants taking the supplements than in those on the placebo. A Finnish study published in 1994 also showed 18% more lung cancers and 8% more deaths in the 29 000 male smokers who took megadoses (20 mg) of beta-carotene daily for five to eight years. Also, beta-catotene has not been shown to confer benefit or harm on heart disease or bowel cancer (MacLennan 1995) (see also Chapter 16).

Although some studies have shown that very high levels of antioxidants provide a degree of protection against free radical damage that leads to cancer, the shortcomings of these experiments were that people were fed only one or two antioxidants to get that effect. At the moment, not enough is known about the full composition of the antioxidant defence system to state that significant protection is provided by one or two antioxidants. Therefore, current antioxidant supplements on the market are based on 'half the story' and could be potentially dangerous. They do not contain the emerging classes of vitamin-like compounds which are suspected to provide the extra health component in fruit and vegetables, such as flavonoids in green tea, wine and soy beans (see Chapter 16). More studies are needed on the doses required of vitamin and vitamin-like compounds which might confer protection against disease. Self-prescribed megavitamin therapy can be dangerous and should only be prescribed by a medical practitioner, based upon sound scientific evidence (see also Chapter 16). Since we do not know exactly what is found in plant foods that confers protection against cancer, it is safer to consume large amounts and a wide variety of plant foods instead of currently available antioxidant vitamin supplements.

Phytochemicals

The protective effect of traditional soy based foods, like tofu (bean curd), has raised the possibility that the weakly oestrogenic factors which they contain, like genistein, may be responsible for this protection. Such compounds may compete with the body's own oestrogens (endogenous oestrogen) and reduce possible adverse effects, but may also work in other ways since they may be antioxidant, immuno-modulatory or anti-angiogenic (see above). Again, salicylates, related to acetyl salicylic acid (aspirin), may be protective against certain bowel tumours (Thun et al. 1993), possibly through effects on cell membranes. Salicylates are found in some foods (Table 32.6). Some people are sensitive to salicylates and therefore may need to be moderate in their intake of these foods. They are likely to be able to achieve a higher intake from foods taken in several small amounts on different occasions rather than as medication (see also Chapter 33). Allium vegetables such as garlic and onions have been found to decrease the risk for gastric and colorectal cancers in epidemiological studies (Fleischauer et al. 2000). However, a case-control study of a Japanese cohort has found the reverse, suggesting the need for further investigation (Tajima and Tominaga 1985). Studies in experimental animals and cultured cells provide strong evidence for cancer prevention (especially skin cancer) by black and green tea and its constituent polyphenols, but evidence from epidemiologic and clinical studies on humans is inconclusive. However, consumption of tea at high temperatures may be a risk for oesophageal cancer (Birt et al. 1999).

Table 32.7 summarises some possibly significant cancer preventive factors in food which are not

Table 32.6 Salicylates in Australian foods

Food	Salicylate content (mg/100 g)	Food	Salicylate content (mg/100 g)
Vegetables		**Vegetables**	
gherkins	6.0	olives	0.3
mushrooms	1.2	lettuce	0.3
capsicums	1.2	carrots	0.2
zucchini	1.0	onions	0.2
eggplant	0.9	cauliflower	0.2
green beans	0.7	potatoes	0.1
tomatoes	0.3–0.6		
Fruits		**Fruits**	
sultanas	7.8	strawberries	1.4
raisins	6.6	apples	1.1
dates	4.5	grapefruit	0.7
cherries	2.8	peaches	0.7
pineapple	2.1	avocado	0.6
oranges	1.7	lychees	0.4
rockmelon	1.5	kiwifruit	0.3
apricots	1.4	lemons	0.2
		passionfruit/pawpaw	0.1
Drinks		**Condiments**	
Benedictine	9.0	thyme	183
port	4.2	oregano	66
tea (2 g leaves/100 ml water)	2–6.5	cinnamon	15
Drambuie	1.6	mint	9.4
Cointreau	0.7	white pepper	6
herbal teas	<1.1	basil	6
coffee (1 g powder/100 ml water	0–0.6	nutmeg	2
beer	0.1	parsley	0.08
		garlic	0.1

Source: Swain et al. 1982

ordinarily regarded as nutrients.

Dietary fibre and refined carbohydrates

Cereal fibre has been shown by several studies to protect against colon cancer. In the Australian Polyp Prevention Project a combination of low fat and wheat bran supplemented diets (providing 11.5 g fibre/day) was associated with fewer new large adenomas over the four years of study (MacLennan et al. 1995). A study from the Arizona Cancer Centre involving 1429 men and women aged 40–80 who had recently had removed an adenoma from the bowel was *unable* to show that taking a fibre supplement (13.5 g fibre/day) would prevent the recurrence of an adenoma. In fact, multiple adenomas were more common in the high fibre group. (Alberts et al. 2000). The different results obtained in these two studies may be explained by the types of fibre supplements used. In the Australian study an unrefined wheat bran as a dietary fibre source was used which was probably also higher in protective phytochemicals (phytoestrogens), vitamin E, B-6 and folate. The American study used a more processed/refined fibre supplement. Furthermore, fibre intake does not appear to account for the reduced risk of colon cancer associated with consumption of fruits and vegetables, and evidence supporting higher consumption of cereal fibre to reduce risk of colon cancer is weak (Willet 1999).

Some epidemiological evidence suggests that eating too much refined cereal products can increase the risk of cancer. The Seven Countries Study has followed the eating patterns of over 12 000 men for almost 30 years. This study has shown a decreased risk of stomach cancer with a high fruit and vegetable intake. Re-analysis of this data has shown that the risk of stomach cancer increases with high intakes of refined grain foods, but not for whole grains and cereals. The

Table 32.7 Food non-nutrients of putative significance in cancer prevention

Component	Relevant cancer
■ salicylates	gut tumours (oesophagus, gastric, colorectal)
■ phytoestrogens/ isoflavones/lignans e.g. soy, peas, wholegrains, extra virgin olive oil	breast, ? prostate
■ monoterpenes/ limonene e.g. citrus fruit	breast, ? various
■ flavonoids/quercetin e.g. fruit, vegetables	skin
■ polyphenols/catechins e.g. green/black tea	skin, ? various
■ diallylsulfides e.g. garlic, onions, leeks, chives	? colon, ? stomach, ? breast
■ isothiocyanates e.g. broccoli, watercress	various
■ tannins e.g. tea, cocoa	skin, lung
■ curcumin e.g. turmeric	various
■ glutathione/whey proteins	colon
■ non-provitamin A carotenoids e.g. lycopene in tomatoes	prostate, various
■ resistant starch (which cannot be digested in small intestine and is fermented in large intestine)	colon

risk remained even when the effects of cigarette smoking were taken into account. The increased risk was not only associated with high grain intakes, but other characteristics of the diet as well. High grain intakes were associated with low intakes of fruit and vegetables—so people with a high intake of grains may have other dietary characteristics which increase their risk (Margje et al. 1999).

Fat quality and meat

Apparent per capita fat consumption in various countries is strongly correlated with rates of cancers of the breast, colon, prostate and endometrium. However, these correlations are limited to animal, but not vegetable, fat. The available evidence most strongly supports an association between high intakes of animal fat and risk of prostate cancer. The link between breast cancer and total fat intake is weak, but mono-unsaturated fat from olive oil may be protective. For colon cancer, the apparently stronger association with red meat than with fat in several cohort studies needs further confirmation. Recent evidence suggests that this might be explained by factors in red meat other than simply its fat content (e.g. haem iron, carcinogens created by cooking). This issue has major practical implications as many food guides around the world support daily consumption of red meat as long as it is lean (see Chapter 38) (Willet 1999).

Conjugated linoleic acid

Omega-6 linoleic acid has been studied as a potential factor in cancer promotion in animal and human studies. However, conjugated linoleic acid (which has conjugated double bonds at carbons 10 and 12 or carbons 9 and 11) has been shown to have antimutagenic activity *in vitro*. It may play a role in protecting against cancers of the skin, stomach and breast. It is found in dairy and meat products (Birt et al. 1999).

Energy balance, growth rate and body size

The role of energy intake in carcinogenesis is a vexed one. There has been a popularised view, derived mainly from rodent experiments, which has argued that energy restriction may decrease the cancer risk and increase longevity. Most of these studies are flawed insofar as extrapolation to humans is concerned because either they are conducted from early life with excessive early mortality, or they do not account for energy expenditure, and therefore energy balance, reflected in body fatness and/or its distribution. Where the full energy equation is available, increased energy throughput (for example, higher energy intakes with no increase in body fatness) has been associated with decreased cancer risk and/or increased life expectancy. Increased energy intake (and possibly its frequency), according to Potter (1990), has in its own right been associated with increased cancer risk at several sites. Again, the quality of extra food intake seems important. The Zutphen prospective study in the Netherlands, conducted by Kromhout and colleagues (Kromhout et al. 1982), showed that increased

energy intake, which included relatively more plant derived food and fish, was associated with lower cancer and total mortality over ten years.

Positive energy balance can contribute to higher growth rates in children, resulting in taller and fatter body size. Several studies have shown that greater height is associated with increased risk of breast cancer, colon and other cancers. Rapid growth rates prior to puberty play an important role in determining future risk of breast and probably other cancers. Early menarche (such as at age twelve as opposed to age seventeen years) is a well-established risk factor for breast cancer. Positive energy balance and over-fatness in adult life contributes to cancers of the endometrium, gall bladder and colon. For breast cancer, there is a reduced risk with greater adiposity prior to menopause; the reverse is true after the menopause (Willet 1999).

Food preservation and cooking

An increased intake of selected plant food and fish may increase certain cancers because of the way they are preserved or cooked (for example, curing, smoking, salting, charring during grilling or barbequing).

Polycylic aromatic hydrocarbons (PAHs)

One group of carcinogenic substances, known as polycylic aromatic hydrocarbons (PAHs), are produced when organic materials such as food or wood are strongly heated. They are widely distributed in our environment, being present in cigarette smoke, exhaust gas and smoked or burnt meat, vegetables and cereals. When wood is burnt, the smoke serves to preserve or flavour food, but some of the PAHs can be absorbed by the food, especially if it is high in fat. In the US and some other countries, virtually all commercially smoked foods are made with liquid smoke. This is a condensate of smoke that has had the harmful chemicals removed. Home smoking of foods does result in addition of the harmful chemicals to the food. Occasional consumption of home smoked foods does not appear to be associated with any known harmful effects and commercially produced smoked foods from big companies probably do not contain enough harmful chemicals to worry about.

Heterocyclic amines

High temperature cooking methods such as deep frying, grilling and possibly roasting of meat, fish, and chicken transforms the protein into weak carcinogenic heterocyclic amines which have been shown in animals to induce cancer. About 40% of Australians have a metabolism that makes the chemicals stronger, increasing the risk of developing bowel cancer. These people would have to eat charred meat regularly before putting themselves at risk.

Nitrosamines

High vitamin C intake is associated with reduced risk of gastric cancer. Vitamin C also prevents the conversion of dietary nitrite and nitrate (in cured meats) to the carcinogenic nitrosamines in the stomach; the nitrosamine pathway for human cancer remain unproven. The protective effects of fruit and vegetables against cancer could be due to their vitamin C content, but a recent study has shown that allium foods (onions and garlic) are also protective. It seems that the active compound could be diallyl sulfide which has been shown to increase the activity of glutathione S-transferase, an enzyme which is involved in the detoxification of carcinogens (Williams and Dickerson 1990).

Pre and probiotics

The consumption of milk has been shown to reduce the incidence of human stomach cancers induced by alkylating agents, while human subjects and experimental animals receiving dietary supplements of *Lactobacillus acidophilus* (found in yoghurt) had significantly lower levels of faecal enzymes that are associated with colon carcinogenesis. *Lactobacillus casei*, *Lactobacillus bulgaricus*, *Lactobacillus bifidum* and *Lactobacillus acidophilus* have also been shown to have anticarcinogenic effects *in vitro* (Bronzetti 1994). Probiotics are defined as live microbial food supplements which benefit the host by improving the intestinal microbial balance (McIntosh 1996) (see Chapter 8). Yoghurt is a traditional and common vehicle for such probiotics (mainly *Lactobacillus* and *Bifidobacteria*). It has been proposed that in the intestine these bacteria may:

1 bind, block or remove carcinogens;
2 inhibit bacteria which directly or indirectly convert procarcinogens to carcinogens by enzyme activity;
3 activate the host's immune system to act against tumours;

4 reduce the intestinal pH, thereby altering microbial activity, solubility of bile acids, mucus secretion;
5 alter colonic motility and transit time (McIntosh 1996).

More studies are needed to confirm the potentially protective effects of fermented food products on carcinogenesis in animals and humans. Other substances which have been shown to have antimutagenic properties *in vitro* in bacterial systems include vanillin (from vanilla pods), cinnamaldehyde (from cinnamon), chlorophyllin (from chlorophyll in plants), selenium (from garlic) and magnesium (Bronzetti 1994).

PREVENTION OF CANCER BY NUTRITIONAL MEANS

Even with the limited evidence available it is possible to propose guidelines for prevention.

It has been estimated that consumption of 400 g/day or more of a variety of fruits and vegetables could by itself, decrease overall cancer incidence by at least 20%. This is a large slice of the estimated 30–40% of cancers that are thought to be preventable by diet, increased physical activity and body weight maintenance. Guidelines for the prevention of cancer by nutritional means have been summarised and adapted from *Food, Nutrition and the Prevention of Cancer: A Global Perspective* 1997 by the World Cancer Research Fund & American Research Institute for Cancer Research, Washington DC in conjunction with the Australasian Nutrition Advisory Council:

1 *Consume a wide variety of biologically distinct foods, especially plant foods.* Focus on plant foods; choose mainly a plant-based diet that is rich in fruits, vegetables, legumes and minimally processed starchy foods.
2 *Eat more vegetables and fruits.* Eat five or more serves of a variety of vegetables and fruits each day. At this point in time, the evidence is strongest for vegetables, (especially for raw vegetables/salads), green vegetables, onion family, carrots, tomatoes and citrus fruits, but these should not be eaten to the exclusion of other vegetables and fruits. Eating a variety will provide the greatest number of protective factors, some of which are yet to be discovered. Convincing evidence of links between diet and cancer is restricted to the protective effect of vegetables, especially for cancers of mouth, pharynx, oesophagus, lung, stomach and colon and moderately strong for the larynx, pancreas, breast and bladder.
3 *Include other plant foods.* Eat seven or more serves of a variety of grains, grain products, legumes, roots and tubers. Prefer minimally processed foods. Limit sugar consumption. Diets high in unrefined starch and fibre may reduce the risk of bowel, pancreatic and breast cancer. Diets high in refined starch and refined sugar may increase the risk of stomach cancer and bowel cancer respectively. Some studies have found that people who have a high intake of sugar (as opposed to moderate) have a lower intake of micronutrients, especially if they are small eaters or their diet is limited in calories. There is no difference in cancer risk between the different types of refined sugars.
4 *If eating meat, use as a condiment—this does not suggest one needs to become a vegetarian.* Red meat can be limited to less than 80 g per day. It may be preferable to choose fish, poultry or meat from non-domesticated animals in place of red meat. For example, the CSIRO 12345+ plan and the National Health and Medical Research Council Core Food Groups recommendation to consume 60–100 g of 'meat and meat alternatives' daily highlights that this amount be consumed from a variety of sources such as red meat, fish, chicken, nuts and legumes (see Chapter 38). Diets high in meat may increase the risk of bowel cancer and possibly breast, pancreas, prostate and kidney cancer. While the fat, protein and iron content of meat—as well as the method used to cook it—have all been considered for possible explanations, it is not exactly known why a high meat diet is linked with an increased risk of cancer. *It may be that meat does not cause cancer per se, but that meat rich diets simply don't provide as much protective plant foods.* As there is only so much room on the plate, individuals can maximise their protection from cancer by filling it first with a variety of plant foods, and if desired, using a small amount of meat for flavouring and to improve the nutrient density of the meal, especially the iron and zinc content. Meat consumed as a condiment will encourage the creation of 'nutritional space' in the diet to

facilitate greater inclusion of plant foods which are protective against cancer. It is recommended to *substitute plant-based meals (for example, legumes, nuts, cereals) for a few meat meals each week.* Clearly, these recommendations do *not* suggest that one must change to a vegetarian diet. However, red meat can be consumed every day if one wishes, providing the serves are 60–100 g, that there is abundant and varied vegetable and fruit intake, and that the meat is not charred during the cooking process.

Reduce total fat intake, especially animal fats. Limit fatty foods, particularly of animal origin; where possible choose low fat dairy products, including low fat fermented milk products; limit polyunsaturated vegetable oils/margarines high in omega-6 fatty acids; prefer a variety of mono-unsaturated oils such as olive, canola, peanut; include intact foods high in unrefined fats, especially omega-3 fats (for example, nuts, seeds, wholegrains, avocado, fatty fish); plant oils are preferable in their natural unrefined liquid form (for example, extra virgin, cold pressed) and not hydrogenated so as to harden them. Reduce total fat intake, but not to less than 15% of energy intake; optimally between 25%–35%, from a variety of fat sources, consumed as near to the basic commodity as possible, for example whole nuts, seeds, grains, fruit.

Avoid salted, cured, smoked and pickled food. These may increase the risk of stomach cancer.

Limit alcohol. Alcohol can increase the risk of cancer, but two or less drinks per day can decrease the risk of cardiovascular disease. There is now convincing evidence that alcohol increases the risk of cancers of the mouth, pharynx, larynx, oesophagus and liver. Regular intake of small amounts of alcohol daily (>1 glass per day) can significantly increase the risk of breast cancer. It may also increase risk of colon and rectal cancers. The risk further increases in people who smoke. However, recommended intakes provide for a limited amount because this takes into account the protective effect of a modest alcohol intake on heart disease risk that is balanced against the general ill effects of alcohol. It is recommended to limit alcohol intake to 2 to 4 drinks per day for men and 1 to 2 drinks per day for women.

8 *Use healthy cooking methods.* Avoid deep frying, charring food, overcooking meat and burning of meat juices if you eat fish or meat (for example as a result of barbequing). Meats that are either charred or exposed to combustion products during cooking may contain cancer-causing polyaromatic hydrocarbons (PAH). Use only occasionally fish or meats that have been grilled in direct flame or that have been cured or smoked. Cured and smoked meats have other compounds incorporated into them during their processing which have also been shown to cause cancer in animals. When cooking, wherever possible, use relatively low temperature methods, such as steaming, boiling, poaching, stewing, casseroling, braising, baking, stir-frying and microwaving. Limit the use of grilling, pan-frying and barbequing, especially for the preparation of meats, or use the following food preparation techniques to minimise formation of carcinogens:
   - remove as much fat as possible;
   - avoid charring the food during cooking;
   - marinate meats/fish in wine, lemon juice, herbs, spices, extra virgin olive oil;
   - cook/serve meats/fish with lemon juice, herbs, spices, fruit chutneys.

9 *Engage in regular physical activity to increase 'energy throughput'.* Keep physically active; include 1 hour of brisk walking each day and a total of 1 hour of vigorous exercise for the week; there is convincing evidence that it can prevent bowel cancer and may keep breast and lung cancer at bay.

10 *Maintain a healthy weight.* Avoid getting too skinny or too fat. Avoid gaining more than 5 kg in adulthood.

11 *Supplements are not necessary.* Results of studies that show a protective effect of foods containing certain nutrients should not be taken to mean that these nutrients, when isolated and taken as supplements, will provide the same benefits for cancer prevention. In some cases there has been an increased risk of cancer in those taking supplements.

NUTRITIONAL MANAGEMENT OF PATIENTS WITH CANCER

The management of patients with cancer is a different proposition to the prevention of cancer. Here, for example, wasting needs to be avoided and foods of increased energy density provided. This may even require an increased intake of certain fats. Other foods

may be needed to reduce the problems of nausea—a reason for using ginger-based food or beverages since ginger is known to possess these properties. Finding palatable foods can be a major challenge. There is uncertainty about what provision of energy or nutrient surplus might do for certain tumours. There is also the possibility that growth factors and growth inhibitors in food may play a role in tumour modulation. Sometimes the major value of nutrition support is to allow other therapies to be successfully used, such as chemotherapy or radiotherapy. Often food and nutrition support is mainly palliative.

SUMMARY

- Cancer is an increasingly important health problem as populations age and succumb less to other health problems. The patterns of cancer are also changing as populations age, people migrate and lifestyles change. Genetics may not play as large a role in cancer risk as once thought. Environmental factors account for about 70% of cancer risk.
- The evidence that nutrition plays a role in the development of many cancers is strong and derived from several lines of enquiry. The mechanisms are less well-understood but involve cancer initiation and post-initiation events of protection or inhibition and of progression and growth control.
- The nutritional risk factors for cancers at different sites vary. Adequate intakes of food, especially vegetables and fruit, and food components—especially antioxidants like phytochemicals, fibre (as in unrefined carbohydrates), prebiotics (like inulin) and conjugated linoleic acid (as in some dairy fats)—may play a role in cancer prevention at various sites. On the other hand, food factors like charred meat (and other foods), quality of dietary fat, food preservation with salt, and cooking techniques by way of barbequing and grilling can increase cancer risk. Positive energy balance, rapid growth rate and larger body size may also increase risk at several sites.
- The evidence is strong enough that physical activity throughout life, the consumption of abundant fruits and especially vegetables, and the avoidance of high intakes of animal fats, alcohol and over-cooked meat in diets low in plant food will reduce risk of human cancer.
- There is a role for nutrition in support of people with cancer.

REFERENCES

Alberts, D.S., Martinez, M.E., Roe, D.J., Guillen-Rodriguez, J.M., Marshall, J.R., van Leeuwen, J.B., Reid, M.E., Ritenbaugh, C., Vargas, P.A., Bhattacharyya, A.B., Earnest, D.L. & Sampliner, R.E. Lack of effect of a high-fiber cereal supplement on the recurrence of colorectal adenomas. Phoenix Colon Cancer Prevention Physicians' Network. *New Engl J Med.* 2000 Apr 20; 342(16):1156–62.

Birt, D., Shull, J. & Yaktine, A. Chemoprevention of cancer. In: *Modern Nutrition in Health and Disease.* M.E. Shils, J.A. Olsen, M. Shike & A. Katherin-Ross (eds). 9th edn. Lippincott, Williams, Wilkins, Baltimore, 1999; 1243–53.

Bronzetti G. Antimutagens in food. *Trends in Food Science and Technology* 1994 Dec; 5:390–5.

Fleischauer, A.T., Poole, C. & Arab, L. Garlic consumption and cancer prevention: meta-analyses of colorectal and stomach cancers. *Am J Clin Nutr* 2000 Oct; 72(4):1047–52.

Fotsis, T., Pepper, M., Adlercreutz, H., Fleischmann, G., Hase, T., Montesano, R. & Schweigerer, L. Genistein, a dietary-derived inhibitor of *in vitro* angiogenesis. *Proceedings from the National Academy of Sciences* 1993; 90(7):2690–4.

Hirayama, T. Diet and cancer. *Nutrition and Cancer* 1979; 1:67–80.

Jensen, O.M., MacLennan, R. & Wahrendorf, J. Diet, bowel function, faecal characteristics and large bowel cancer in Denmark and Finland. *Nutr Cancer* 1982; 4:5–19.

Kromhout, D., Bosschieter, E.B. & De Lezenne Coulanders, C. The inverse relation between fish consumption and 20-year mortality from coronary heart disease, cancer and all causes. The Zutphen Study. *Lancet* 1982; 2:518–21.

Lester, I.H. & NHMRC Expert Panel. Morbidity and mortality associated with diet-related disease. In: *Australia's Food and Nutrition*. Australian Government Publishing Service, Canberra, 1994; 218–26.

Lichtenstein, P., Holm, N.V., Verkasalo, P.K., Iliadou, A., Kaprio, J., Koskenvuo, M., Pukkala, E., Skytthe, A. & Hemminki, K. Environmental and heritable factors in the causation of cancer—analysis of cohorts of twins from Sweden, Denmark and Finland. *NEJM* 13 July 2000; 343(2). <http://www.nejm.com/content/2000/0343/0002/0078.asp>.

McIntosh, G.H. Probiotics and colon cancer prevention. *Asia Pacific J Clin Nutr* 1996; 5(1).

MacLennan, R., Macrae, F., Bain, C., Chapuis, P., Lambert, J., Newland, R.C., Ngu, M., Russell, A., Ward, M., Wahlqvist, M.L. & the Australian Polyp Prevention Project. Randomized trial of fat, fibre and beta-carotene intake to prevent colorectal adenomas. *J Nat Cancer Institute* 1995; 87:1760–6.

McMichael, A.J., McCall, M.G., Hartshorne, J.M. & Woodings, T.L. Patterns of gastrointestinal cancer in European migrants to Australia: the role of dietary change. *Int J Cancer* 1980; 25:431–7.

Margje, C.J.F. et al. Consumption of plant foods and stomach cancer mortality in the Seven Countries Study. Is grain consumption a risk factor? *Nutrition and Cancer* 1999; 34(1):49–55.

Potter, J.D. The epidemiology and prevention of pancreas cancer. In: *Cancer Prevention Vital Statistics to Intervention*. W. Zatonski et al. (eds). Interpress, Warsaw PA, 1990.

Swain, A., Dutton, S. & Truswell, A.S. Salicylates in Australian foods. *Proc Nutr Soc Aust* 1982; 7:163.

Tajima, K. & Tominaga, S. Dietary habits and gastro-intestinal cancers: a comparative case-control study of stomach and large intestinal cancers in Nagoya, Japan. *Jpn J Cancer Res* 1985; 76:705–16.

Tattersall, M. *Preventing Cancer*. Australian Professional Publications, Sydney, 1988.

Thun, M.J., Namboodiri, M.M., Calle, E.E., Flanders, W.D. & Heath, C.W. Aspirin use and risk of fatal cancer. *Cancer Research* 1993; 53:1322–7.

Wahlqvist, M.L. Nutritional factors in carcinogenesis. *Asia Pacific J Clin Nutr* 1993; 2:141–8.

Wei, Y.Q., Zhao, X., Kariya, Y., Fukata, H., Teshigawara, K. & Uchida, A. Induction of apoptosis by quercetin: involvement of heat shock protein. *Cancer Research* 1994; 54:4952–7

Willet, W. Diet, nutrition and the prevention of cancer. In: *Modern Nutrition in Health and Disease*. M.E. Shils, J.A. Olsen, M. Shike & A. Katherin-Ross (eds). 9th edn. Lippincott, Williams, Wilkins, Baltimore, 1999; 1243–53.

Williams, C.M. & Dickerson, J.W. Nutrition and cancer—some biochemical mechanisms. *Nut Res Rev* 1990; 3:75–100.

World Cancer Research Fund & American Research Institute for Cancer Research. *Food, Nutrition and the Prevention of Cancer: A Global Perspective*. Washington, DC, 1997.

FOOD AND NUTRITION

Australasia, Asia and the Pacific

Second Edition

Edited by
Mark L. Wahlqvist

Contributors
Madeleine Ball
David R. Briggs
Patricia A. Crotty
Gwyn P. Jones
Antigone Kouris-Blazos
Louise B. Lennard
Richard S.D. Read
Iain Robertson
Ingrid H.E. Rutishauser
Mark L. Wahlqvist
Naiyana Wattanapenpaiboon

Thanks to Antigone Kouris-Blazos for her editorial and technical assistance.

ALLEN&UNWIN

First published in 1997
Second edition published in 2002 by
Allen & Unwin Pty Ltd
83 Alexander Street, Crows Nest, NSW 1590 Australia
Phone: (61 2) 8425 0100
Fax: (61 2) 9906 2218
E-mail: info@allenandunwin.com
Web: www.allenandunwin.com

National Library of Australia
Cataloguing-in-Publication entry:

Food and nutrition: Australasia, Asia and the Pacific.

2nd ed.
Includes index.
ISBN 1 86508 692 4

1. Food. 2. Food analysis. 3. Food—Australian.
4. Food—New Zealand. 5. Nutrition.
6. Nutrition—Requirements. 7. Nutrition
Australia. 8. Nutrition—New Zealand.
I. Wahlqvist, Mark L.

641.3

Set in 10/12 Bembo by Asset Typesetting Pty Ltd
Index compiled by Russell Brooks
Printed by South Wind Productions, Singapore

10 9 8 7 6 5 4 3 2

Contents