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Nutrition and cancer

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OBJECTIVES

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

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 regulation of cell death or 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 41.1.

Table 41.1 Mechanisms of carcinogenesis

Stages	I Initiation	II Post-initiation		
		A Promotion Inhibition (reversibility)	or	B Progression (→undifferentiation) Growth control
Mechanisms	**Mutational event**			
genotoxic chemicals	specific tumour viruses	radiation		
Role of food/nutrition	Yes	Yes		Yes

Table 41.2 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	obesity diabetes	obesity CHD CVD diabetes

CVD: cerebrovascular disease
CHD: coronary heart disease

Table. 41.3 Large bowel cancer and diet in Scandinavia

	Finland		Denmark	
	Rural	**Helsinki**	**Rural**	**Copenhagen**
Incidence rate (per 105)				
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

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 anti-oxidant, vitamin E as anti-oxidant, 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 40). What is eaten may encourage *progression* (by various growth 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 soya 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 41.2). They may have companion non-cancer chronic non-communicable disease.

An even more detailed examination of the diet–cancer relationship within a region or culture can be helpful (Table 41.3) (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 more from dairy products than in Denmark which 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

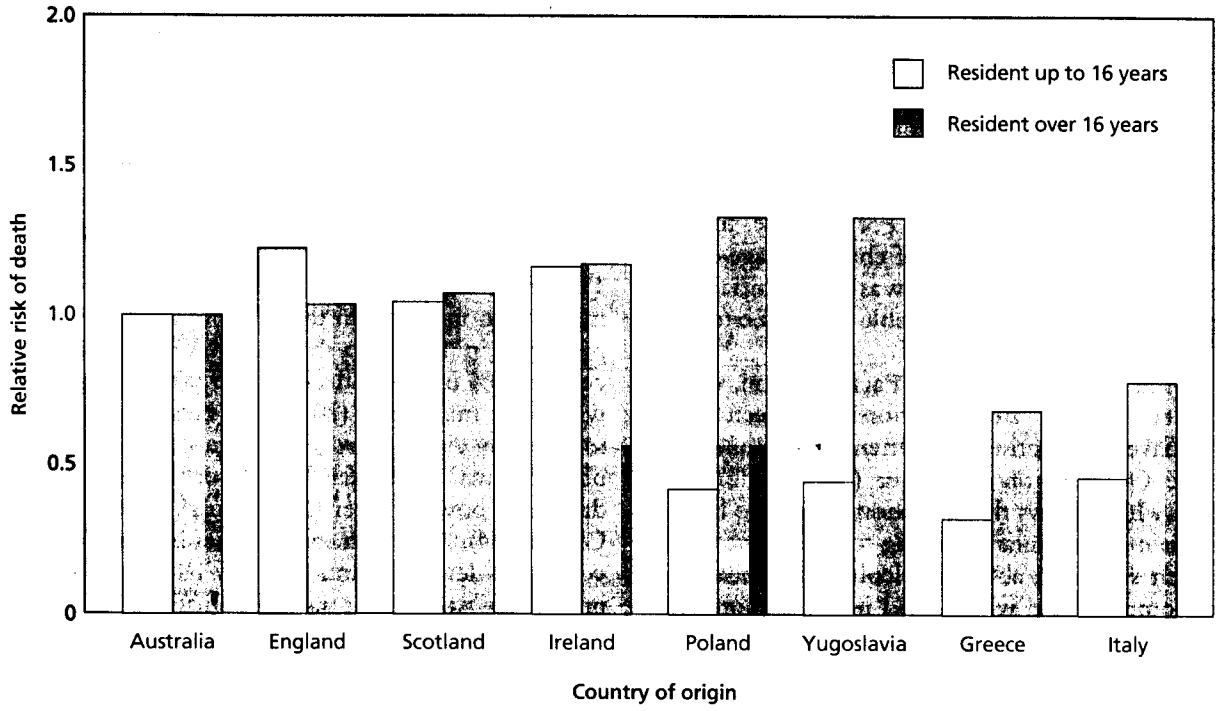

Figure 41.1 Age–sex standardised relative risk of death by length of residence in Australia: rectal cancer

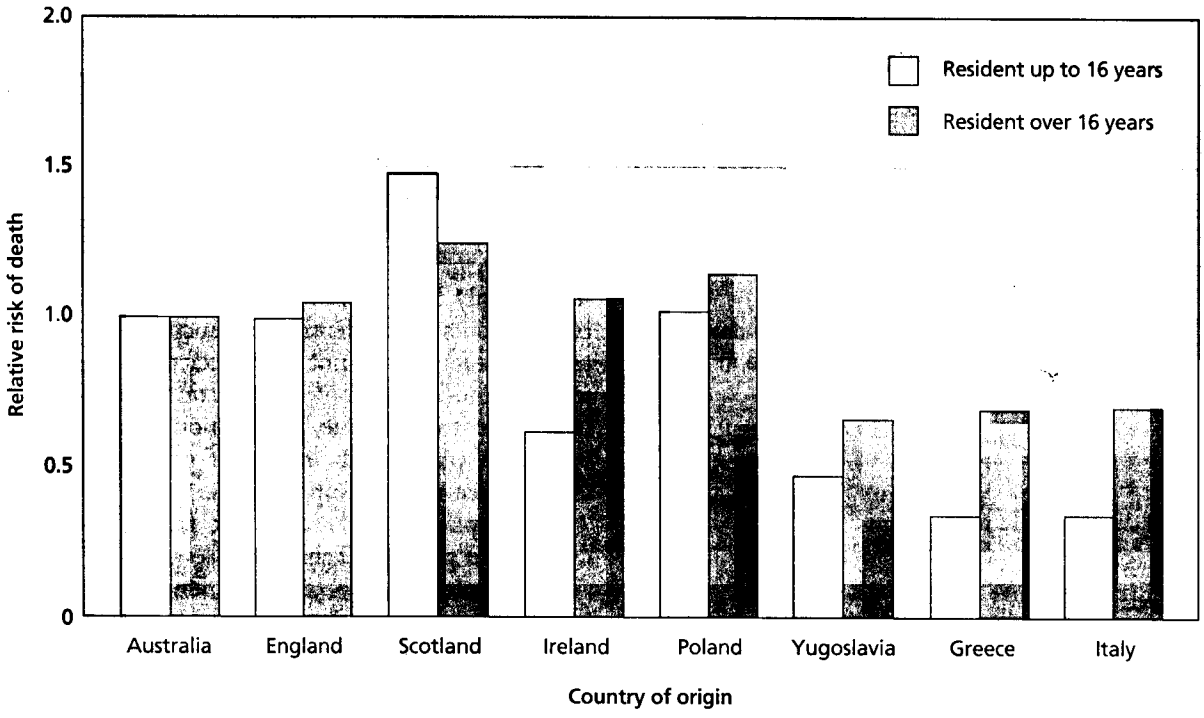

Figure 41.2 Age–sex standardised relative risk of death by length of residence in Australia: colon cancer

bowel (colo-rectal) cancers among first generation of 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 41.1 and 41.2).

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 41.4) (Lester and NHMRC, 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 41.2). The lifestyle which allows this transition 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 anti-oxidants, see Chapter 24) were considered the obvious choices to simulate the properties of fruit and vegetables, but it could well have been any 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 told 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 24). Although some studies have shown that very high levels of anti-oxidants have 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 anti-oxidants to get that effect. At the moment, not enough is known about the full composition of the anti-oxidant defence system to obtain significant protection from one or two anti-oxidants. Therefore, current anti-oxidant supplements on the market only contain 'half the story' and could be potentially dangerous. They are not providing 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 soybeans (see Chapter 24). More studies are needed on the doses required of vitamin and vitamin-like compounds which confer protection against disease. Self-prescribed mega vitamin therapy can be dangerous and should only be prescribed by a medical practitioner, based upon sound scientific evidence (see also Chapter 24). 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 anti-oxidant vitamin supplements.

Examples of nutritional risk factors for certain cancers are given in Table 41.5.

Where protection or detriment applies this is indicated by +, and the strength of this relationship by the number of + signs. Where there is a possible effect, this is indicated by a ? sign (Wahlqvist, 1993). The case for these risk factors is derived from several lines of evidence. These may be experimental in

Table 41.4 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 1982–1985.

Table 41.5 Examples of nutritional risk factors for certain cancers

Breast cancer	Protective	Detrimental
1 energy balance	+	
body fat (total fat and distribution)		
• pre-menopausal		
• post-menopausal		+
physical activity	+	
2 fat intake (> 20% energy)		+
3 fat quality (↑polyunsaturated fats) (mono-unsaturated fats may reduce risk)		+
4 alcohol (> 5g/day)		+
5 soy products (increase traditional products e.g. tofu, tempeh) ? phytoestrogens	+	
6 meat intake		+
7 reproductive life span (e.g. menarche to menopause) and/or its nutritional determinants (e.g. correction of childhood malnutrition); breastfeeding reduces the risk, especially with longer total duration	?	?
8 vitamin A from food	+	
Colorectal cancer		
fruits and vegetables	+	
wheat bran/cereal fibre	+(high fat diet)	+(low fat diet)
dairy components		
ca	+	
vitamin D	+	
whey proteins (from dairy products)	+	
yoghurt (bacteria lactobacillus/bifidus)	?+	
alcohol		+
fat		+
? meat, ? barbecued meat		+
Pancreatic cancer		
energy		+
caffeine		?
cholesterol		+
trypsin inhibition		+
alcohol		?
build (larger)		+
fish oil	?+	+
protein (and high fat)		+
Prostate cancer		
vegetables	+	
• green leafy and yellow	+	
• soy	?	
fat intake		+
body mass		+
? muscle mass		+
? physical activity		+
cadmium		?+
Gastric cancer		
charred foods (e.g. grilled, barbecued meat)		+
salty foods (e.g. olives, salted vegetables and meats)		+
pickled vegetables (e.g. gherkin)		+
smoked foods (e.g. ham, fish)		+
cured foods containing preservative nitrate/nitrite (e.g. salami, sausages)		+
sesame oil	+	
allium foods (onions, garlic)	+	
lack of foods containing vitamin C		+

Table 41.5 (cont.)

Gastric cancer	Protective	Detrimental
factors encouraging certain gastric microflora, like helicobacter pylori, which may lead to atrophic gastritis		+
Ovarian cancer		
galactose		+
• more common in women who drink milk every day.		
• ? genetic predisposition through galactosaemia		
? obesity		?+
fruits and vegetables	+	
fat intake		+

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.

The mechanisms by which food and food components influence the development of cancer still often lack detailed understanding (Table 41.1). 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 40). The immunodeficiency associated with ageing, with HIV-positivity, and with transplantation of organs where immunosuppression is required, increases the risk of cancer.

The protective effect of traditional soya 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 their adverse effects, but may also work in other ways since they may be anti-oxidant, immunomodulatory or anti-angiogenic (see above). Again, salicylates, related to acetyl salicylic acid (aspirin) may be protective against certain bowel tumours (Thun et al., 1993) and colleagues in the American Cancer Society), possibly through effects on cell membranes. Salicylates are found in some foods (Table 41.6).

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 43).

Table 41.7 summarises some possibly significant cancer preventive factors in food which are not ordinarily regarded as nutrients.

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 are 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 (e.g. 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 (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

Table 41.6 Salicylates in Australian foods

Food	Salicylate content (mg/100g)	Food	Salicylate content (mg/100g)
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

over 10 years. In other communities, an increased intake of selected plant food and fish may increase certain cancers because of the way they are preserved or cooked (e.g. curing, smoking, salting, charring during grilling or barbecuing). One group of carcinogenic substances in smoked and burnt foods, known as polycyclic aromatic hydrocarbons (PAHs), are produced when organic materials such as food or wood are strongly heated. 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. The formation of PAHs can be minimised by removing as much fat as possible and not charring the food during cooking (Wahlqvist and Briggs, 1991).

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 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 sulphide 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).

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

Table 41.7 Food non-nutrients of putative significance in cancer prevention

Component	Relevant cancer
salicylates	gut tumours • oesophagus • gastric • colorectal
phytoestrogen	breast prostate
glutathione/whey proteins	colon
non pro-vitamin A carotenoids	various
flavonoids	various
tannins	skin lung
curcumin (in tumeric)	various
enzyme-inducers (e.g. in broccoli)	colon
resistant starch (which cannot be digested in small intestine and is fermented in large intestine)	colon

Chapter 4). 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 antitumorigenesis
4 reduce the intestinal pH, thereby altering microbial activity, solubility of bile acids, mucus secretion
5 alter colonic motility and transit time (McIntosh, 1994).

More studies are needed to confirm the potentially protective effects of fermented food products on carcinogenesis in animals and humans (McIntosh, 1996). Other substances which have been shown to have antimutagenic properties *in vitro* on 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. Essentially we need:

1 a wide variety of biologically distinct foods especially plant foods and, where possible, low fat dairy products, including low fat fermented milk products
2 a diet that is low fat (<<20% to 25% energy intake)
3 a modest intake of omega-6 fatty acids (found in polyunsaturated oils and margarines), with regular intake of omega-3 polyunsaturated fats (mainly found in deep sea fish) and preference for vegetable fat of mono-unsaturated origin (olive oil) or in intact food (e.g. nuts, cereals)
4 to avoid deep frying
5 regular physical activity to increase 'energy throughput'
6 to avoid salted, cured, smoked and pickled food
7 a modest alcohol intake, preferably with food.

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 experience lifestyles change.
- 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.
- Cancer prevention is at least, in part, presently available by nutritional means.
- There is a role for nutrition in support of those with cancer.

REFERENCES

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

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

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

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

McMichael AJ, McCall MG, Hartshorne JM & Woodings TL. Patterns of gastrointestinal cancer in European migrants to Australia: the role of dietary change. *Int J Cancer* 1980; 25:431–7.

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

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

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

Thun MJ, Namboodiri MM, Calle EE, Flanders WD & Heath CW. Aspirin use and risk of fatal cancer. *Cancer Research* 1993; 53:1322–7.

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

Wahlqvist ML & Briggs DR. *Food Questions and Answers: Sort the facts from the fads to help you choose a healthy diet*. Penguin Books, Melbourne, 1991, p. 134.

Wei YQ, 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

Williams CM & Dickerson JW. Nutrition and Cancer—some biochemical mechanisms. *Nut Res Rev* 1990; 3: 75–100.

FOOD AND NUTRITION

Australasia, Asia and the Pacific

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