Chapter 3
Nutrition

Let thy food be thy medicine and thy medicine be thy food.
Hippocrates.
In Chinese medicine, diet therapy is the highest form of medicine.
Various Chinese medical texts.

In this chapter we explore the following:

- Evidence of an association between diet and cancer
- Cancer risk factors associated with diet including obesity and diabetes
- How foods can heal, including their effects on cancer pathogenesis
- Incorporating dietary advice into the Ultimate Consultation
- 14 Key Dietary Principles including foods to include and foods to avoid.

Introduction

We are what we eat. From both the ancient Greeks and the ancient Chinese (and of course many other cultures), we receive the same wisdom—food is a source of medicine. We are alive because of the various food sources available to us, at a very basic level. But that doesn't mean we are all alive and well.

For people with cancer, ensuring that the foods eaten on a daily basis are good foods is very important to give them the best possible chance of overcoming cancer. A healthy patient will do better than an unhealthy one and good nutrition is one of the essential pillars of health, along with stress reduction, exercise, sunlight and sleep. The practice of mindfulness and daily creative sessions are also very important. If a person is not feeling good about themselves, however, they probably won't choose good foods, so it is vital that the patients address stress and unload it. The mind–body connection is extremely important, as you can see from just some of the evidence about stress and cancer in Chap. 2.

Cancer is reflective of a state of imbalance within the body. Poor food choices can set up a pro-inflammatory state systemically, and systemic inflammation is part

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of the pathogenesis of cancer, as well as many other chronic diseases. Good food choices can assist by first not adding to the inflammatory process, and second, may help counteract many of the pathways involved in the pathogenesis of cancer.

Our earth has provided us with the means to achieve wellness. Many plant foods found in nature have anti-cancer properties: the scientific evidence of how particular foods and/or the active constituents within them interrupt the various pathways involved in cancer is established and growing. Plants have many potentially active constituents within them which act synergistically and likewise the combination of certain foods can have a synergistic effect. The emphasis therefore should be on a healthy and balanced diet.

In This Chapter

This chapter will look first at some of the evidence of an association between diet and cancer, as well as evidence of associations between particular diets and better health outcomes. The evidence of an association between overweight and obesity and cancer is then examined, before then looking more closely at cancer pathogenesis, to understand how foods can address many of the events involved in cancer. We will then discuss 14 Key Dietary Principles, encompassing foods to avoid and foods to add to a patient's diet.

In this book, we will cover some of the basics of diet and nutrition only. For more in-depth discussions, readers are referred to the many good books on nutrition that are available such as David Wilkinson's *Can Food Be Medicine Against Cancer* and Kenneth Block's *Life Over Cancer*. Pieces of wisdom from the ancient Chinese that pertain to diet as well as life more generally can be found in Peter Deadman's book *Live Well Live Long*.

Evidence of the Association Between Diet and Cancer

The figures may differ a little from publication to publication, however, it has been estimated that only 5–10% of cancer is due to genetic defects. Up to 30–35% of cancer-related deaths are estimated to be linked with diet, 25–30% are due to smoking, 15–20% due to infections and the rest due to other factors such as stress, physical inactivity, radiation, and environmental pollutants [7]. Even if a person has a genetic defect that may increase risk of cancer, by protecting themselves with a healthy lifestyle and diet, the disease won't necessarily manifest.

The link between diet and cancer has been revealed by findings of a large variation in cancer rates between countries and correlations with diet and observations of changes in cancer rates with migration [7, 42]. When people migrate from countries known to have low rates of specific cancers (such as Asian countries where the incidence of prostate cancer is 25 times lower and rate of breast cancer 10

times lower) to countries with high rates, adopting the diet and lifestyle of the new country of residence, cancer rates in these people increase substantially [7].

Evidence of Protective Effects of Particular Diets Against Cancer

Studies on Diets High in Vegetables and Fruits

There is substantial research that indicates the protective effect of diets high in vegetables and fruit against cancer and their role in the prevention of disease recurrence [33, 42, 58, 153, 164, 217, 218, 241]. See Table 3.1 for some examples. However, it is important to be aware that there have also been many studies which have not found an association between diets high in vegetables and fruits, or low in fats, with cancer. These might seem counterintuitive to common sense; however, the individual studies need to be interpreted carefully, and the diets of study populations scrutinised. As argued by Campbell and Campbell [42], some large studies which have investigated the relationship between particular dietary factors and cancer risk have made erroneous conclusions because their study populations were

Table 3.1 Studies that support positive impact of vegetables and fruit

• The Iowa Women's Health Study of almost 42,000 middle-aged women found that consumption of all vegetables and fibre were inversely associated with risk of colorectal cancer, with a 27 and 20% reduced risk comparing the groups with highest intake with lowest respectively [241]
• High consumption of vegetables, particularly cruciferous vegetables (though not fruit), was found to be associated with a reduced risk of prostate cancer [58]
• The Black Women's Health Study found that total vegetable intake was associated with a significantly decreased risk of oestrogen-negative/progesterone-receptor-negative breast cancer (though not overall breast cancer risk) and there was a non-significant trend of an inverse association between breast cancer risk and intake of cruciferous vegetable intake and carrot intake [33]
• Increased fruit and vegetable consumption was associated a greater recurrence-free survival in women with breast cancer, as measured by the biomarker plasma carotenoids [218]
• A review of observational cohort studies (1985–2002) found that there was a positive association between intake of vegetables, fruit and their micronutrients and survival in five of eight cohort studies of breast cancer survivors [217]
• Another study of 1901 early-stage breast cancer patients that women following a diet characterised with high intakes of fruits, vegetables, whole grains, and poultry had statistically significant decreased risk of overall death as well as death from non-breast cancer causes [153]
• A population-based cohort study of 609 women with epithelial ovarian cancer who were observed for up to 5 years found a significantly reduced risk of death in women who had a higher intake of vegetables before diagnosis (25% reduction) and higher intake of cruciferous vegetables [180]

eating diets high in animal-based foods (even though low in fat) and the studies were trying to hone in on one nutrient or food at a time [42]. The limitations of scientific research must be borne in mind—if studies are not well set out, the inherent reductionist nature of research may miss important findings. Whole dietary patterns are more likely to be much more important.

Vegetarian Diets

Epidemiological studies indicate that those on vegetarian diets, in particular vegan diets, tend to live longer than meat-eaters. A study of Seventh Day Adventists found that there was a 12% reduction in risk of death from all causes in vegetarians compared with non-vegetarians [194]. An earlier study in 34,192 Seventh Day Adventists found that cancers of the colon and prostate were significantly more likely in non-vegetarians (increased risk of 88% and 54% respectively). Also, those who ate meat frequently had a higher risk of bladder cancer [102]. In addition, the intake of legumes was negatively associated with risk of colon cancer (in meat-eaters) and risk of pancreatic cancer, and higher consumption of all fruit or dried fruit was associated with decreased risks of lung, prostate, and pancreatic cancers [102]. However, what also needs to be considered here is the social/family therapy provided within close-knit communities, as this might be just as important as the foods eaten.

Mediterranean Diet

The Mediterranean Diet is also known to be associated with better health outcomes including reduced total mortality and cardiovascular disease risk [26]. A review of observational studies indicated that it is probably protective against cancer also [263]. The diet is characterised by a high intake of olive oil and low intake of saturated fats, high consumption of fruit, vegetables, nuts, cereals and legumes (that in the past were largely unrefined), moderate consumption of ethanol (mostly as red wine at meals), moderately high consumption of fish (depending on proximity to the sea), low consumption of meat and meat products, and low-moderate intake of milk and dairy products (and then mostly in the form of cheese and yoghurt) [253].

The European Prospective Investigation into Cancer and Nutrition (EPIC) study investigated the dietary, lifestyle and other characteristics of more than half a million people in Europe before a diagnosis of cancer or another chronic disease. The study of 25,623 Greek men and women found that not only were there benefits of adopting the diet in terms of a significantly reduced incidence of cancer, but even adopting some aspects of the diet was sufficient to lower the incidence of cancer. The closer the adherence to the diet, the lower the incidence and risk of cancer.

What was very interesting was that although the Mediterranean Diet was strongly and inversely associated with cancer risk, when they examined the association between the individual components of the diet, they did not find any significant associations between these and cancer risk. This could suggest that there are synergisms between the components of the diet that are important (though other explanations relate to how data is combined in research) [26]. Other studies have also found that a high degree of adherence to this diet is associated with significantly lower mortality from cancer as well as coronary heart disease [253].

Lessons from 'The China Study'

The China Study was a correlation study of women and men living in 65 counties in 24 provinces of rural China. It stands as one of the most significant ecological studies in nutrition of the twentieth century, led by eminent researcher Dr. T. Colin Campbell. Some of the findings of this study, together with research from other sources that are published in the book entitled *The China Study* (Wakefield Press), provide evidence-based arguments that a diet high in animal-based foods is implicated in particular cancers. They also remind us of the methodological shortcomings of much of the research into nutrition which has focussed on individual nutrients or foods rather than examine diet in the more holistic sense.

A startling difference was found between rural China and the typical western diet in the U.S. The rural Chinese diet had less fat (14.5% of calories in rural China vs. 34–38% in the US), more dietary fibre, more iron, and less total protein. In rural China, 9–10% of total calories were consumed as proteins, with only 10% from animal-based foods (the majority coming from plant sources of protein). In contrast 15–17% of total calories of the American diet were from protein, and more than 80% of it was from animal sources. What was extremely interesting was that the rural Chinese diet, high in plants and low in animal protein, was *higher* in total calories than the U.S. diet, yet they were slimmer—average body mass index in rural Chinese was less than in the U.S. and this wasn't explained by differences in physical activity [42].

The Social Context of Eating Is a Missing Link in Research

What is missing from studies on diets such as the Mediterranean Diet is consideration of the context for eating. The Mediterranean Diet is not perfect—it contains preserved meats, recently pronounced as carcinogenic, and there are cakes and ice creams in the mix of what is eaten too (the latter are not listed as features of the diet however). What is likely to also be protective is the family structure that provides the context for eating in these cultures and regions of the world. Perhaps it is the

social support that eating within a family environment that is more important? The social context of eating may be healing and protective in itself. It may even compensate for some of the poorer food choices. We won't know for sure until we have a 'university study', but we can hypothesise.

Happiness is contagious and can positively impact on others. The Framingham Heart Study found that a friend who becomes happy and who lives within about 1.6 km (one mile) of another person increases the chance that the other person is happy by 25%; the effect is even greater (42%) when the friend lives within half a mile (0.8 km). Similar effects were found in relation to siblings who live within a mile (14% increase) and next door neighbours (34%) [103]. The positive changes that can occur within the immune system of people in the company of others, and other factors including Vitamin D levels, physical activity level and other behavioural factors are rarely considered in research designs, yet arguably they need to be. Research designs do need to consider foods and nutrition within a broader behavioural and social context. Food for thought (pardon the pun).

Key Points:

- The social context of eating may be healing and protective in and of itself
- Research needs to consider the social contexts of eating and the potential impact on health.

Overweight, Obesity and Cancer

Overweight and obesity are risk factors for cancer, diabetes and Metabolic Syndrome (which are themselves risk factors for cancer), development of insulin resistance (visceral adiposity), as well as hypertension, stroke and coronary heart disease [27, 115, 178, 184]. Many cancer patients are overweight and therefore may have co-morbidities. Addressing weight, through healthy food choices, is likely to have many health benefits and this will be discussed later in the chapter.

Stress and Weight

It's important to remember that if a person is overweight or obese, there are usually a multitude of actors involved. For example, if someone is stressed, they may eat more, leading to increased cortisol being released into the bloodstream, as well as insulin. Figure 3.1 shows some of the factors that may be involved:

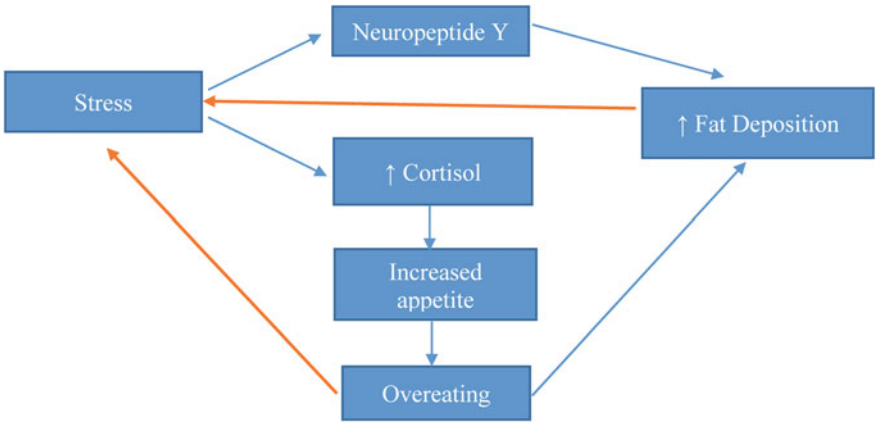

Fig. 3.1 Stress and overweight

The Link with Cancer

Being overweight or obese is a risk factor for cancer occurrence. In the year 2000, obesity was estimated to contribute to an estimated 14% (men) and 20% (women) of cancer-related mortality in the U.S. [40]. In 2007, an estimated 34,000 new cases in men (4%) and 50,500 new cases in women (7%) were due to obesity [182]. Body mass index (BMI) is significantly associated with higher death rates due to the following cancers: oesophagus, colon and rectum, liver, gallbladder, pancreas, kidney, non-Hodgkin's lymphoma and multiple myeloma. There is a significant trend of increased risk of death with increasing BMI for cancers of the stomach and prostate in men and breast, uterus, cervix, and ovary in women [40].

Cancer sufferers who are obese tend to have poorer outcomes in terms of increased risk of all-cause mortality and cancer-specific mortality [182]. Those with a body mass index (BMI) of at least 40 have been found to have death rates from all cancers combined that are 52% and 62% higher for men and women respectively compared to those of normal weight [40].

Breast cancer

Women with breast cancer who are overweight or obese are significantly more likely to die of breast cancer than lean women [272]. Women who are obese at breast cancer diagnosis have a 33% higher risk of recurrence and mortality compared with women who have normal weight [209]. Several observational studies have found an association between post-diagnosis weight gain and higher risk of recurrence and mortality which was independent of BMI at the time of diagnosis [34]. In women with Stage 1–3 breast cancer, being overweight or obese has a negative impact on recurrence-free survival, overall survival and breast cancer-specific survival; diabetes also has a negative impact on overall survival and

recurrence-free survival [137]. Overweight and obesity also increase the likelihood of progression including metastasis in triple negative breast cancer following surgical resection [54].

Postmenopausal breast cancer survivors who were overweight or obese had higher levels of sex hormones (estrone, estradiol, testosterone) than lighter women, providing a potential link between adiposity and breast cancer [173]. Overweight and obesity and lack of physical activity are all associated with increased inflammatory markers including CRP, interleukin-6, interleukin-1, serum amyloid A and tumor necrosis factor α [129, 205]. Inflammation is a key part of the cancer terrain.

More than 65% of breast cancer survivors are overweight or obese [137], and unfortunately the majority of women who are in the normal weight range gain weight after diagnosis [262]. This is clearly not something that is desirable.

Metabolic Syndrome and Diabetes as Risk Factors for Cancer

Metabolic Syndrome is a risk factor for several forms of cancer including liver, colorectal, and bladder cancer in men, and endometrial, postmenopausal breast, rectal and colorectal in women [87]. Diabetics have a higher risk of several cancers including pancreatic, liver, breast, colorectal, kidney, bladder, endometrial and breast cancer and non-Hodgkinson's Lymphoma, and mortality is also increased [265].

In one study of women with early-stage breast cancer, women with the highest fasting insulin levels had approximately twice the risk of distant recurrence and over three times the risk of death compared with women in the lowest fasting insulin group, and the effect of insulin on survival was independent of body mass index [109].

Insulin resistance has been implicated in the pathogenesis of cancer: chronically elevated insulin can lead to tumor growth [41] and insulin resistance has been linked to breast cancer development [139, 243]. When insulin is elevated, it leads to increased IGF-1. IGF-1 and insulin, which are both understood to be growth factors, then down-regulate apoptosis and promote cell division [126]. Elevated fasting insulin levels have been found to be associated with distant recurrence and death in women with early breast cancer; insulin has been found to be correlated with body mass index, which in turn was found to be significantly associated with distant recurrence and death [109].

Benefits of Weight Loss in Cancer

There is clear evidence of benefits of weight loss in cancer and risk factors for cancer. Weight loss, through lifestyle approaches that combine changes to diet and increased physical activity, can have important health benefits on some of the risk factors for cancer that may also be co-morbidities (e.g. insulin resistance, Metabolic

Table 3.2 Weight loss benefits for cancer and cancer risk factors

• A recent review found that several weight loss and exercise programs in healthy women as well as breast cancer survivors were associated with reductions in insulin levels of 10–30% [130]. This is important since lowering of insulin by 25% has been found to be associated with a 5% absolute improvement in breast cancer mortality [109]
• The Women's Nutrition Intervention (WIN) Study, though not specifically investigating impact on weight, found that a low fat diet was associated with significantly reduced weight loss and decreased breast cancer recurrence in women with breast cancer. The effect on breast cancer recurrence was stronger in women with estrogen-negative breast cancer. Other mechanisms are likely to be involved in breast cancer (other than sex hormones) including adipokines, IGF-1, insulin resistance and inflammatory biomarkers [31]
• A study of physical activity and caloric restriction intervention in healthy postmenopausal women found that lower caloric intake as well as physical activity and lower body mass index were all independently associated with significantly lower mean fasting insulin levels [51]
• A study showed that insulin resistance has been found to improve significantly after weight loss, albeit via gastric band surgery [120]
• The Diabetes Prevention Program study of people at risk of diabetes investigated the impact of a lifestyle intervention program that included a weight reduction goal and physical activity. Those in the lifestyle intervention group had significantly greater weight loss than the two control groups and that they developed significantly less diabetes (incidence reduced by 58%) at the end of the study than the Metformin Group (incidence reduced by 31%) or the placebo group. Both lifestyle intervention and Metformin were associated with lower blood glucose levels after one year (Diabetes Prevention Intervention Group 2002)

Syndrome and diabetes), and on some of the underlying cancer pathways involving insulin and IGFs. See Table 3.2 for some of the studies.

Caution needs to be taken however: sudden weight loss in cancer patients may increase the risk of clinical deterioration, possible due to the effects of increased metabolic end-products and nutrient depletion.

How Foods Can Heal

As mentioned previously it has been estimated that up to 30–35% of cancers are linked to diet [7]. This is worth remembering, as it means quite a lot of cancer can be prevented through healthy food choices.

Dr. T. Colin Campbell and his colleagues originally conducted studies in rats to investigate the impact of animal-based foods including dietary protein on the initiation and promotion of cancer. These and other animal studies indicate some very important findings in relation to diet and cancer pathogenesis including the following:

- Nutrition is far more important in controlling cancer promotion than the dose of the initiating carcinogen
- Nutrients from animal-based foods (including casein in milk) increased tumor initiation and development and nutrients from plants decreased their development

- A plant-based diet encourages more physical activity and discharges calories as body heat instead of storing them as body fat [42].

Whilst these studies are in animals, nonetheless they are helpful in understanding how diet can impact the development of cancer which might be applicable to humans. See the book *The China Study* [42] for some very interesting reading.

Foods Acting on Pathways Involved in Cancer Pathogenesis

There are specific foods and their active constituents that have an action on the pathways involved in cancer pathogenesis, including cancer metabolism, cell cycle control, apoptosis, inflammation, hormonal balance, angiogenesis and metastasis [252]. Some foods can assist by boosting the immune system, whilst others work as protective food chemicals. The specific actions of particular foods in relation to cancer pathogenesis will be discussed throughout this chapter.

Plants as Antioxidants or Modulators?

What is not well understood is that plants and some of their active constituents are able to modulate various activities within the body. For example, cocoa can enhance the function of normal cells but destroy cancer cells [138]. Omega-3 oils in fish, for example, can enhance immunity in persons with depressed immunity, and can normalise or modulate hyperactive immunity in people with allergic conditions or autoimmune disorders [143].

Research is now showing that nutrients that have previously been thought to act as antioxidants are actually acting in a different way in protecting the body against, or combatting cancer. For example, Vitamin C has traditionally been known of as an antioxidant; however, it has been shown to be able to destroy cancer cells in vitro without neutralising the efficacy of chemotherapy and in human studies [32]. Here Vitamin C is clearly not acting as an antioxidant under these circumstances. Vitamin E has also been shown, in vitro, to assist in the destruction of cancer cells when irradiated (whilst helping to preserve normal cells). Antioxidants are discussed in more detail in Chap. 7.

An Alternative Theory of Carcinogenesis and Implications for Diet

Before we turn to how to incorporate dietary advice into an integrative consultation, it's worthwhile noting what is considered the dominant theory of carcinogenesis, and describing (very briefly) another theory that has been forming for many decades

that challenges it, for it does have some implications for diet. The Somatic Mutation Theory of Cancer which has dominated the last one hundred years of scientific research into cancer posits that cancer is primarily due to genetic mutations. The 'Metabolic Theory of Cancer', originating with Warburg and later developed further by others including Pederson and more recently Seyfried [233], posits that cancer is a metabolic disease first and foremost, rather than a genetic disease. According to this theory, the mitochondria have become damaged, leading to defective respiration. Genetic mutations occur downstream from this event, not prior to it. Seyfried sets out convincing scientific evidence that in cancer cells, the mitochondria have become damaged and fewer in number, and instead of using the oxidative phosphorylation pathway, utilise the less efficient glucose fermentation pathway [55, 232, 233]. This theory fundamentally challenges the direction of oncology research which has primarily focused on trying to understand and characterise genetic mutations. It also has profound implications for metabolic therapies that could be developed.

The 'Ketogenic Diet' was developed on the basis of this theory. The diet is characterised by caloric restriction, low in carbohydrates and protein, and the rest of the diet consisting of fats. The justification for this is that cancer cells have a high need for glucose, and when glucose is restricted, the cancer cells are forced to compete with healthy cells for available glucose. Healthy cells are able to switch to burning ketone bodies, but cancer cells are unable to, which creates metabolic and oxidative pressure [55]. Pre-clinically and in case studies, there is evidence that the diet can slow tumor growth [55].

For more information readers are referred to two excellent books, *Tripping Over the Truth: the Return of the Metabolic Theory of Cancer Illuminates a New and Hopeful Path to Cure* (Travis Chistofferson), an easy read, and for the serious science, *Cancer as a Metabolic Disease* (Thomas Seyfried) (see Reading Recommendations at the end of the book).

There are, of course, many other diets that have been devised for cancer sufferers. Readers are referred to other sources for information on these. We will now examine what kinds of information may be included in discussions with cancer patients in relation to eating and foods.

Incorporation of Dietary Advice into the Ultimate Consultation

There are a few simple goals in the Ultimate Consultation when it comes to nutrition:

- Goal 1: Sharing information on the role of eating and diet in health
- Goal 2: Finding out what the cancer patient habitually eats
- Goal 3: Sharing information about foods to avoid and foods to include in the diet.

It is suggested that you put any dietary advice in writing (e.g. as part of a Wellness Plan) and review within 3 months. Generally, people forget most of what they have been told within 3 months [212]. Professor Sali gives his patients printed notes to take home with them, summarising key information and giving them sample breakfast, lunch and dinner ideas. In addition, it's wise to remember that dietary changes should be doable: if changes are too difficult to make due to unaffordability or lack of access to particular foods, or if diet recommendations are too rigid, this can add stress to the patient. This is not desirable. The changes should be able to be sustained—rigid diets can simply make people miserable and be counterproductive. Finally, in the end the patient has to be responsible for making changes.

Key Points About Dietary Advice

- Put any dietary advice in writing and review within 3 months
- Dietary changes should be do-able and sustainable
- The patient is responsible for making changes to diet.

Goal 1. Sharing Information on the Role of Eating and Diet in Health

The first part of this chapter set out evidence in relation to how diet might impact both positively and negatively in relation to cancer. Some of these general facts and figures could be shared with the patient, emphasising what positive changes can be made going forward that will assist the patient in achieving better health overall. Here are some general topics that you could start with, before getting into discussions about specific foods:

- **How the mind–body connection comes into play in eating**: The importance of the mind–body connection in association with eating habits can also be discussed, including how stress can lead to unhealthy eating habits such as overeating or making poor food choices. Generally speaking, if a person is not feeling good about themselves, they will probably not make healthy choices about food. They may also use food as a means of comforting themselves, contributing to overeating. Thus, the root cause of stress and unhappiness needs to be addressed.
- **Changing diet is about forming new, healthier habits**: Diets are habits and often simply repetitions of cultural and/or family patterns. Changing diet is about practising eating those foods that are most beneficial for health. Making changes will take discipline, not unlike the discipline of athletes or sportswomen/men and their commitment to training.

- **Relationship between overweight/obesity and cancer**: Where relevant, the relationship between overweight/obesity and cancer outcomes, plus other diseases that are risk factors for cancer (e.g. diabetes, Metabolic Syndrome) can be discussed, again with an emphasis on what positive changes can be made to achieve more favourable outcomes. It may be useful to mention some facts and figures from studies that have demonstrated the benefits associated with weight loss (Table 3.2), as this may help motivate the patient to make changes.
- **Why good food is important during chemotherapy/radiation therapy**: If the patient is going to undergo chemotherapy or radiation therapy, they should be advised that it is important no additional stresses are placed on the body by ingesting foods that set up pro-inflammatory conditions. People receiving chemotherapy or radiation therapy are already receiving a toxic insult to their bodies, so it is important not to add further toxicities through poor food choices.
- **Why the context of eating is important**: An important aspect of healthy eating is the context within which it is done. When eating can be done in a relaxed atmosphere, with loved ones, there are the added benefits of social therapy that can be tremendously positive. The health benefits of diets such as the Mediterranean Diet are likely to be as much about the context of eating within a family support system as some of the foods eaten, though this aspect of nutrition, the context of eating, is not something that is investigated in most of the published studies on nutrition. Yet, it is likely to be very important. Eating with someone can be a good opportunity for important unloading of stress.
- **How foods can address some of the cancer pathways**: The clinician can share some basic information about the underlying processes involved in cancer pathogenesis, and how foods are able to assist in addressing some of these processes. Again, by empowering patients with basic information, it gives them essential knowledge as to how and why making changes to diet might benefit them.

Goal 2. Finding Out What the Patient Habitually Eats

In the consultation, it will be important to understand a patient's food habits which can be done simply by asking the patient what they usually eat, as a rule, for breakfast, lunch and dinner. Also, you can ask them whether they skip meals, what they snack on, what beverages they have daily and how many cups approximately (which will give you an idea of liquid intake). For more details, you can ask the patient to complete a 5-day diet diary in which they record everything they eat and drink for 5 days, including at least one day on a weekend (since diets can change on weekends). Frequency of consumption of foods that are unhealthy, including fast foods is important: eating an occasional fast-food meal is unlikely to be

problematic; however, eating them frequently and in large quantities will most certainly be and will most likely lead to weight gain plus changes within the body that can contribute to cancer (and other disease) pathogenesis.

Completing a diet diary is, in and of itself, educational for patients and that itself may encourage learning and change. What we eat is largely habitual, usually forged over a lifetime and often following family patterns of eating. Changing diet means changing habits and practising a new habit, one that is healthier. The key is to empower the patient with information and the knowledge that they can change.

Key Points

- If a person is not feeling good about themselves, they are more likely to make poor food choices. The root cause of stress and unhappiness needs to be addressed.
- Completing a 5-day diet diary is educational and may encourage learning and change.
- Diet is habitual. Changing diet means changing habits and practising a new habit, one that is healthier. This will require discipline.

Goal 3. Sharing Information about Foods to Avoid and Foods to Include in the Diet

In beginning a conversation about what foods can be added to diet and which ones to avoid the clinician can begin with talking about some overarching dietary recommendations. Key recommendations from the *World Cancer Research Fund and American Institute for Cancer Research Second Expert Report* [276] include the following:

- Eat mostly plant-based foods
- Limit intake of red meat and avoid processed meat
- Limit consumption of energy-dense foods and avoid sugary drinks
- Limit consumption of salt
- Avoid mouldy cereals and legumes/pulses.

Then one can move on to talking about 14 Key Dietary Principles, set out in Table 3.3, working through each of these systematically. Professor Sali has printed patient notes that summarise most of these principles that he gives to the patient to take home with them. He uses these as a framework to work through information about diet.

The remainder of this chapter will focus on each of these 14 Dietary Principles.

Table 3.3 Fourteen dietary principles

1. Eat regularly and enjoy meals
2. Eat organic foods where possible and avoid genetically modified foods
3. Eat a rainbow diet of colorful foods, with plenty of fresh vegetables and fruit daily
4. Limit red meat
5. Incorporate healthy dairy products
6. Reduce overall consumption of (unhealthy) fats
7. Consume healthy fats and oils and avoid unhealthy ones
8. Keep hydrated but choose your drinks wisely
9. Avoid excess sugar, artificial sweeteners and salt
10. Avoid foods containing acrylamides
11. Eat dark chocolate
12. Eat for your gut microbiome
13. Avoid foods that interfere with sleep
14. Pay attention to food cooking and storage methods

Principle 1: Eat Regularly and Enjoy Meals

When a person has cancer, it is prudent to remember, particularly when there is cachexia or when they are undergoing treatment such as chemotherapy that appetite is disrupted and nausea may be prevalent. It is important that eating is perceived as enjoyable, as much as is possible under the circumstances. Adhering to strict diets, however, nutritionally justifiable (and many are not) may simply be counterproductive if the poor person is miserable. Sometimes too much emphasis can be placed on diet to the point that the person and their loved ones living with them are stressed out about food. We think that this is counterproductive.

As much as possible, meals should be regular and eating should be done in an atmosphere that is not rushed, and allows for plenty of time to chew (an important and often neglected part of the digestive process), bringing people together in a positive atmosphere (social therapy). The coming together over a meal is an opportunity to relax, enjoy company and unload stresses and the positive benefits of this should not be underestimated. A study found that when people were paired up and fed various foods, when they ate the same foods, rapport was better [274].

For those with poor appetite and/or nausea (which can be the experience of those having chemotherapy), including ginger in the meal or having a cup of ginger tea 30–60 min prior to meals can help improve appetite.

Principle 2: Eat Organic Foods Where Possible and Avoid Genetically Modified Foods

Where possible, organic foods are vastly superior to non-organic foods for a few reasons. First, there is evidence that they contain higher amounts of nutrients. Second, organic foods don't contain the added pesticides and other contaminants

that most commercially grown fruit and vegetables have which can add a toxic load to the body [21].

A recent review of nearly three decades of epidemiologic research (44 papers) on the relationship between Non-Hodgkin Lymphoma (NHL) and occupational exposure to agricultural pesticides found that several herbicides and insecticides were positively associated with NHL and two herbicides were associated with a subtype, B Cell Lymphoma [227]. Whilst occupational exposure in the agriculture industry is arguably different to the kind of exposure through eating foods that have been sprayed with pesticides, this nonetheless should sound a cautionary bell.

The Danger of Genetically Modified Organism (GMO) Foods

Genetically modified organism (GMO) foods are a recent phenomenon and whether they can cause cancer in humans is not substantiated (yet); however there is concern about their potential to cause harmful effects on the body. The major debates on health concerns around GMOs are based on theoretical considerations and animal experiments [72]. The problem has been that there are no epidemiological studies (human or animals) to support a claim either way, and part of the issue is that there is a lack of labelling and therefore sources of evidence in GMO-producing countries [72].

Major cultivated GMO foods are soy, corn and oilseed rape or canola. These plants have been modified genetically to tolerate and/or produce one or more pesticides, and contain residues of these (most of which are Roundup residues, a major herbicide used throughout the world) [72]. Table 3.4 sets out foods most and least prone to contamination with pesticide residues.

Animal research has shown that three different types of genetically modified maize were associated with signs of hepatorenal toxicity in rodents, and effects on the heart, adrenal, spleen and blood cells were also found [71]. A controlled study in which 200 rats were fed with maize treated with Roundup or Roundup-contaminated water for 2 years found that the rats had disturbances in liver and kidney biochemical markers and testosterone and estradiol levels at 15 months, and at the end of the study, hepatorenal deficiencies and female

Table 3.4 foods more and least prone to contamination with pesticide residue

Foods prone to contamination with pesticide residue	Foods least prone to retaining pesticides
Celery, cucumbers, tomatoes, cherry tomatoes, capsicum, cucumbers, snap peas, potatoes, hot peppers, spinach and kale, and the following fruit: apples, strawberries, peaches, grapes, cherries and nectarines [85, 273]	Avocados, sweet potato, cauliflower, cabbage, eggplant, asparagus, sweet corn, peas, sweet peas, asparagus, eggplant, and onions (broccoli is also considered reasonably clean) and the following fruit: grapefruit, cantaloupe, honey dew melon, pineapples, mangoes, paw, and kiwi fruit [86, 273]

mammary tumors (3.25 more than the control group at 700 days) associated with premature death [229].

The evidence about GMO foods is slowly gathering. We know herbicides/insecticides are poisons and there is some indication of serious adverse effects in animal studies. Thus, it is best to avoid GMO foods where possible, particularly when one has an illness such as cancer. This is of course made more difficult if food products are not labelled as to whether or not a product contains GMO foods or not. It is thus incumbent on all of us to put pressure on our own governments to change this.

Switching to Organic Foods

As much as possible, patients should try to make the switch to organic foods. However, these are more expensive in general, and not as readily sourced. If it is not possible to switch entirely to organic foods, an option may be to choose to buy organic those vegetables that are more prone to chemical contamination. Another option is to buy as organic foods those foods that are readily available and therefore there probably won't be as much of a price differential (between organic and non-organic). If organic foods cannot be purchased, patients should be advised to wash vegetables and fruits carefully. This will, at least, remove some of the contaminants on the surface of the vegetables and fruits though it won't affect the chemicals that are absorbed into the produce.

When buying meat, again if possible, patients should be advised to buy organic to avoid the hormones that are added to the diet of cattle, sheep, pigs and chickens, which make their way into the meat of the animals and thereby into our bodies. It's also important to remember that even if you eat good food, if you eat too much of it, that will not be helpful either.

Principle 3: Eat a Rainbow Diet of Colorful Foods, with Plenty of Fresh Vegetables and Fruit Daily

Eating a healthy diet with a variety of different colored vegetables and fruits helps ensure that the right balance of nutrients, including vitamins and minerals, is consumed. Vegetables, fruits, legumes, nuts and seeds provide a variety of micronutrients and other bioactive compounds, and many have anti-cancer properties. The health benefits of fruits and vegetables are also understood to be partly due to the presence of phytochemicals including carotenoids, sulphoraphanes, flavonoids, salicylates, phytosterols, saponins, glucosinolates, polyphenols, phytoestrogens, lectins and others. Several of these phytochemicals act as antioxidants, preventing damage to cells, protein and DNA [276].

Choose Vegetables and Fruits in Season

When choosing vegetables and fruits, it is generally better to choose those that are in season. According to Chinese medicine diet therapy principles, it is better to eat cooked vegetables and foods in the cold months and not eat raw foods such as salads, which are better eaten in the hotter months. On a practical note, foods in season are generally cheaper and fresher. Fruit is best eaten before the main meal when one is hungriest, as it can help prevent overeating or choosing less healthy options.

Recommended Daily Servings of Fruit and Vegetables

The Australian Dietary Guidelines recommends eating five–six servings of vegetables and two servings of fruit each day for men and (non-breast-feeding) women [17]. Fruit is high in glucose. In general, when eating fruit it is better to eat the whole fruit (as opposed to drinking the juice) as this slows the release of glucose into the blood, thereby helping to reduce spikes in blood glucose levels. Eating the whole fruit also helps satiate the appetite.

Recommended Daily Servings of Vegetables and Fruit

- 5–6 servings of vegetables
- 2 servings of fruit.

Evidence of Protective Effect of Vegetables and Fruits Against Cancer

An early review of 206 human epidemiologic studies and 22 animal studies found consistent evidence for a protective effect of increased vegetable and fruit consumption across a range of cancers including stomach, oesophagus, lung, oral cavity and pharynx, endometrium, pancreas, and colon [242]. A study of 61,463 Swedish women found an inverse relationship between total fruit and vegetable consumption and colorectal cancer risk; those who consumed less than 1.5 servings of fruit and vegetables per day had a 65% increased risk of developing colorectal cancer compared with those who consumed more than 2.5 servings [249]. Systematic reviews have found an inverse association between dietary fibre intake and overall cancer risk [53].

Fruit and vegetables are an important source of fibre, as are cereals and grains. The relative contribution towards protection conferred by fruits and vegetables

through the fibre component compared to other constituents is not clear. A systematic review found that a high intake of total daily fibre, and wholegrains and cereal fibre, but not vegetable or fruit fibre, was associated with a decreased risk of colorectal cancer [15]. In another systematic review of breast cancer, again there was a decreased risk of cancer associated with higher overall dietary fibre intake, but not individually for fruit or vegetable fibre (the only one that demonstrated individually a significant inverse association was soluble fibre) [16]. The Nurses' Health Study did not find an association between colorectal cancer risk and fibre intake from fruit or vegetables; however the Health Professionals' Follow-Up Study did find an inverse association between the intake of fruit fibre and distal colon adenomas, but not from cereals or vegetables [206]. Similarly, another systematic review of 14 cohort studies found that those consuming 800 g/day total fruits and vegetables or more had a 26% lower risk of distal (but not proximal) colon cancer compared to those consuming <200 g/day [148]. Dietary fibre is discussed further in Section "Dietary Fibre".

Many of the micronutrients within vegetables and fruits including carotenoids, folate, vitamin C, vitamin D, vitamin E, quercetin, pyridoxine, and selenium have been found, in systematic reviews, to be associated with decreased risk of a range of cancers [276]. The World Cancer Research Fund and American Institute for Cancer Research Second Expert Report concluded that foods containing selenium 'probably protect' against prostate cancer; and there is 'limited evidence' that they are protective against stomach and colorectal cancers. The report states that there is also 'limited evidence' to support that foods containing pyridoxine protect against oesophageal and prostate cancers and that Vitamin E-containing foods protect against oesophageal and prostate cancers [276].

In rural Chinese people, lower blood Vitamin C levels were associated with higher incidence of cancer, in particular cancers of the oesophagus, nasopharynx, breast, stomach, liver, colorectal and lung [42]. Fruit intake was inversely associated with oesophageal cancer and cancer rates were 5–8 times higher in those places where fruit intake was lowest [42]. Stomach cancer has also been found to be significantly higher when blood levels of beta-carotene, plasma levels of selenium and green vegetable intake were lower [147].

Fruits as Sources of Protective Nutrients

Fruits are important sources of protective nutrients (such as Vitamin C plus phenols and flavonoids, beta-carotene and other carotenoid antioxidants), other potentially bioactive phytochemicals, as well as fibre [276]. According to the World Cancer Research Fund and American Institute of Cancer Research Second Expert Report: Food, Nutrition, Physical activity and the Prevention of Cancer: A Global Perspective, foods that are high in Vitamin C probably protect against oesophageal cancer and those containing dietary fibre probably decrease colorectal cancer risk. The report found probable evidence for fruit in reducing risk of cancers of the

mouth, pharynx, larynx, oesophagus, lung and stomach, and suggestive evidence for cancers of nasopharynx, pancreas, liver, and colo-rectum [276].

Vitamin C's role in cancer prevention includes being able to trap free radicals and reactive oxygen molecules (thereby protecting against oxidative damage), regenerating other antioxidant vitamins including Vitamin E, inhibiting formation of carcinogens and protecting DNA against mutagenic attack. Fruits such as apples and grapefruit contain high levels of flavonoids. Flavonoids have antioxidant effects and can also inhibit carcinogen-activating enzymes. Phytochemical antioxidants in fruit can also reduce free-radical damage generated by inflammation [276].

Berries

Berries, particularly strawberries and raspberries, are rich in ellagic acid which has been found, in laboratory studies, to prevent several cancers including bladder, skin, lung, oesophageal and breast. It works via a number of mechanisms including acting as an antioxidant, deactivating specific carcinogens and slowing the reproduction of cancer cells. Strawberries contain flavonoids which act via similar mechanisms. Blueberries contain anthocyanosides which are believed to be the most powerful antioxidants discovered [276]. Black raspberries have been found, in rat studies, to work by inhibiting cell proliferation, suppressing inflammation, blocking angiogenesis and promoting apoptosis [244].

Crucifers

Broccoli and other crucifers are able to arrest cancer cell division, invasion of tissues and angiogenesis, can aid apoptosis, enhance the expression of good genes and block oestrogen [273]. Broccoli has been found to contain glucoraphanin, a glucosinolate precursor of sulforaphane, which has been found to have anti-cancer properties, and 3–4-day-old broccoli sprouts have up to 20 times the amount of this phytochemical compared to the mature plant. Sulforaphane induces carcinogen-detoxifying enzymes, activates apoptosis and blocks cell cycle progression [247], and may target cancer stem cells (responsible for initiating and maintaining cancer, and contributing to drug resistance and recurrence) via several mechanisms including modulation of NF-κB and other pathways [162].

Cooking Hint: Broccoli
How broccoli is cooked is important. Cooking destroys one of its critical enzymes, and therefore it should be lightly steamed only for 3–4 min or stir-fried briefly; boiling for only 5 min reduces the activated nutrient substantially [273].

Table 3.5 Sources of common carotenoids

Sources of both β-carotene and α-carotene	Other sources of α-carotene	Lycopene
Pawpaw, rock melon, mangoes, oranges, carrots, sweet potato, squash and other yellow/orange fruits and vegetables plus some of the green vegetables such as spinach and kale	Peas, green beans, avocado and broccoli	Tomatoes and some other red-colored plants including watermelon, apricot, guava, pink grapefruit and peaches

Based on data from Wilkinson [273], Tanaka et al. [245]

Colorful Veggies

Carotenoids are natural fat-soluble pigments that are responsible for the bright coloration of particular plants and animals. There are several carotenoids in vegetables including α-carotene, β-carotene, lycopene, β-cryptoxanthin, lutein, zeaxanthin, capsanthin and crocetin. Citrus fruits contain B-cryptoxanthin and marine sources of carotenoids include astaxanthin, β-carotene, zeaxanthin, canthaxanthin, fucoxanthin and lycopene. β-Carotene is the major source of vitamin A as a provitamin A carotenoid [245]. Some sources of common carotenoids are set out in Table 3.5.

Studies have found an association between diets rich in carotenoids and cancer protection. A systematic review of 18 studies (over one million women) found that a carotenoid-rich diet was associated with a lower risk of oestrogen receptor-negative breast cancer (but not oestrogen receptor-positive breast cancer) [289]. Another meta-analysis combining 8 cohort studies found that women with the highest levels of lycopene, β-carotene, and α-carotene had a 22%, 17% and 13% reduced risk of breast cancer respectively compared with women with the lowest levels; risk reduction capacity of carotenoids was greater for oestrogen receptor negative cancers than for oestrogen receptor-positive cancers [82].

In vitro and in vivo studies have demonstrated strong anti-tumor effects of several carotenoids including β-carotene, α-carotene, lycopene, lutein, zeaxanthin, and others [245]. In vitro research has confirmed that synergism between compounds is important. In a study of hormone-dependent prostate cells, combinations of carotenoids or carotenoids and polyphenols and/or other compounds were found to work synergistically to inhibit the androgen receptor activity and activate the Electrophile-Responsive/Antioxidant-Responsive Elements (EpRE/ARE) system. The activation of the EpRE/ARE system was up to four times higher than the sum of the activities of the single ingredients, providing evidence of synergism [165].

Lycopene

Lycopene has a high antioxidant capacity and has been found in some in vitro studies to selectively arrest cell growth and induce apoptosis in cancer cells (without harming normal cells). Lycopene can affect several IGF-1-activated

signalling pathways, PDGF (platelet derived growth factor) and VEGF (vascular endothelial growth factor) signalling pathways, and there is evidence that it has anti-inflammatory actions and can prevent angiogenesis, invasion and metastasis in several cancers [252].

In epidemiological studies, lycopene has been found to be protective against several cancers including prostate, breast, lung, and colon [108]. However, there are other studies that have not found associations. For example, a prospective study of almost 40,000 women found that there was no association between lycopene in diet and plasma lycopene levels and risk of breast cancer in middle-aged and older women [230]. Clinical studies in men with prostate cancer have demonstrated that lycopene supplementation may be a useful adjuvant treatment. A study found that 80% of men who took 30 mg of lycopene/day for 3 weeks prior to radical prostatectomy had smaller tumors than controls, and their PSA levels had decreased by 18% compared to the control group which had increased by 14% [149].

Cooking Hint to Enhance Lycopene Absorption
To enhance the absorption of lycopene, oil or fat is needed—so add some olive oil to cooked tomatoes/tomato paste/tomato sauce to get the full benefit of lycopene from tomatoes.

Garlic

Garlic (Allium sativum) contains at least 33 different organosulfur compounds, plus amino acids, vitamins and micronutrients. The allyl sulphur constituents are understood to be responsible for its health benefits [187] which include positive effects on cardiovascular health and immunity. Recent research indicates that fermented or aged garlic can reduce blood pressure in hypertensive people and has the potential to modulate slightly elevated cholesterol levels [216].

Garlic and risk of cancer

The weight of evidence in the epidemiological literature supports the contention that garlic consumption is associated with reduced colorectal and gastric cancer [226]. Systematic reviews have found that raw or cooked garlic has a protective effect on colorectal cancer [95, 187] and gastric cancer [95, 293]. One of the reviews also found reduced risk for other cancers including prostate, oesophageal, larynx, oral, ovary and renal (but not gastric, breast, lung and endometrial cancers) [95], though a recent one did not find that raw or cooked garlic or garlic supplements lowered colorectal cancer risk [125]. The Iowa Women's Health Study that analysed the diets of almost 42,000 middle aged women found that intake of garlic was inversely associated with risk of colon cancer, as were intakes of all vegetables and dietary fibre [241].

Mechanisms of action of garlic on cancer pathogenesis

How garlic exerts its effect in preventing cancer is not fully elucidated. Whilst it may be ascribed partly to its anti-cancer and protective nutrient/antioxidant effects, it may also be related to garlic's underlying effect on the immune system. Studies on the effect of garlic on the immune system have revealed somewhat conflicting results regarding whether it stimulates pro-inflammatory or anti-inflammatory activity; however, overall the evidence suggests that garlic elicits anti-inflammatory immune responses. There is evidence that garlic can strengthen the immune system within the tumor micro-environment against the immunosuppressive activity of emerging tumors and it has been proposed that garlic is able to act as an immune modulator, shifting the balance from a pro-inflammatory and immunosuppressive environment to an enhanced anti-tumor response [226]. A study of 50 people with inoperable colorectal, liver or pancreatic cancer found that taking aged garlic extract for 6 months improved immune function, significantly increasing number and activity of NK (natural killer) cells [131]. Garlic also acts as a prebiotic, benefiting the gut microbiome.

Animal research indicates that garlic and its allyl sulphur constituents are able to affect colorectal cancer pathways via a variety of mechanisms including induction of apoptosis, DAS inhibition of colorectal cell proliferation, blockage of cell growth, blockage of angiogenesis, inhibition of carcinogen-induced DNA adduct formation, enhancement of carcinogen-metabolising enzymes, inhibition of COX-2 expression, scavenging carcinogen-induced free radicals and inhibition of lipid peroxidation [187]. Other constituents of garlic are also important in its protective effects against cancer including kaempferol, selenium, vitamins A and C, arginine, and fructooligosaccharides [187].

Cooking Hints for Garlic

Heating garlic without peeling inactivates alliinase (which promotes the formation of beneficial sulphur compounds) and substantially decreases or eliminates its active properties. Garlic should be peeled and chopped and allowed to stand for 15–20 min so it can release the enzyme alliinase; then the active agents formed are subsequently not destroyed via normal cooking methods [276].

Mushrooms

Mushrooms have a number of beneficial properties including being immune-boosting, pain-killing, anti-diabetic, anti-viral and antimicrobial, and have anti-cancer properties. They are able to activate the immune system, act as antioxidants, block oestrogen, inhibit invasion and metastasis, stimulate apoptosis, and may prevent recurrences caused by resistant stem cells [199, 273]. Mushrooms

are useful as an adjunct to chemotherapy and radiation therapy as they are able to counter many of the side effects including nausea, bone marrow suppression, anaemia, and lowered resistance [199].

Shiitake mushrooms are common and easy to procure. Shiitake mushroom (*Lentinula edodes*) produces lentinan, a β-glucan which can suppress leukaemia cell proliferation [199]. In vitro and animal studies have found that shiitake extracts have immune-stimulatory [133], anti-proliferative [133], cytotoxic [286], anti-mutagenic [67] and anti-tumor activity [270]. It has also been found to improve immune function in healthy humans [63] and decrease the incidence of chemotherapy-associated side effects in patients with advanced gastrointestinal cancer [191].

Ganoderma lucidum has demonstrated anti-cancer properties, and is used in Chinese herbal medicine. A systematic review of five randomised controlled trials (373 subjects) found that patients incorporating *G. lucidum* in their anti-cancer regime were 1.27 times more likely to respond to chemotherapy or radiation therapy compared to those without. It was found to stimulate immune function by increasing CD3, CD4 and CD8 lymphocyte percentages, and marginally elevate NK cell activity. Those taking *G. lucidum* were also found to have better quality of life after treatment compared with the controls [135].

Principle 4: Limit Red Meat

There is convincing evidence that red meat should have a very limited place within diet and that consumption increases the risk of some cancers. Processed meat should be eliminated from diet as it is carcinogenic. There is no clear data on whether meat from grass-fed animals is better than non-grass-fed animals.

Epidemiological Evidence About Meat

Epidemiological research that has compared diets between countries and death rates from various diseases gives us an insight into patterns in relation to diet that are important. Such studies have demonstrated that increased animal protein consumption is associated with higher rates of heart disease, breast cancer and colorectal cancer [42]. For example, over 40 years ago research indicated that in countries with higher meat, animal protein and sugar consumption and less consumption of cereal grains, rates of colon cancer in women was higher [9]. Similarly, over three decades ago, a study of 142,857 Japanese women over 40, followed for 10 years, found that the risk of breast cancer was 8.5 times higher in women of high socioeconomic class who ate meat daily compared with women of low socioeconomic class who did not [122].

Other research has demonstrated that in countries with higher animal fat (but not plant fat) intake age-adjusted death rates for breast cancer are higher [47]. The

China Study found that higher animal protein intake and animal protein-related blood markers were significantly associated with increased prevalence of cancer in Chinese families [42].

A report from the International Agency for Research on Cancer (IARC) states that eating red meat was found to be associated with an increased risk of colorectal, prostate and pancreatic cancer, and processed meat was found to be associated with stomach cancer [127]. Processed meats include ham, bacon, sausage, hot dogs, corned beef and some delicatessen meats (processing refers to the treatment of the meat to preserve it or enhance the flavour, and includes salting, curing, fermenting, and smoking).

Red Meat and Processed Meat Are Causes of Cancer

A statement that a food causes cancer is much stronger than simply stating there is an association. Published in 2007, the World Cancer Research Fund and American Institute of Cancer Research's Second Expert Report found that red meat is a convincing cause of colorectal cancer, with a substantial amount of evidence from cohort and case–control studies showing a dose–response relationship supported by evidence for plausible mechanisms in humans [276]. It also found 'limited evidence' for red meat as a cause of oesophageal, lung, pancreatic, and endometrial cancers [276]. The report also found 'convincing evidence' that processed meats are a cause of colorectal cancer and 'limited evidence' that processed meats are a cause of stomach, prostate, lung and oesophageal cancer [276].

Classification of Meat as Carcinogenic

Processed meats have now been classified by the International Agency for Research on Cancer (IARC) as 'carcinogenic to humans (Group 1)', and red meat (which includes beef, pork, lamb, goat, mutton, veal, horse) has been classified as a 'probably carcinogenic to humans (Group 2A)' [127]. A systematic review of over 800 studies found that each 50 g portion of processed meat eaten daily increased the risk of colorectal cancer by 18% and each 100 g portion of red meat eaten per day increased the risk by 17% [127].

Potential Mechanisms of Red Meat in Cancer Development

Potential underlying mechanisms for an association between red meat and cancer include generation of potentially carcinogenic N-nitroso compounds by the stomach and gut bacteria. The cooking of some red meats at high temperatures can produce

heterocyclic amines and polycyclic aromatic hydrocarbons which have been linked with cancer. Haem in red meat promotes the formation of N-nitroso compounds and also contains iron, and free iron is one of the most powerful catalysts that can lead to free radical production. In addition, excessive iron can induce hypoxia signalling, and activate oxidative transcription factors and pro-inflammatory cytokines [276].

It is known that oestrogen levels are a critical determinant of the risk of breast cancer [281]. Campbell and Campbell argue that higher dietary fat is associated with higher blood cholesterol and these, in addition to higher female hormone levels, are associated with earlier age of menarche and increased breast cancer [42]. They argue that a diet rich in animal-based foods will maintain high levels of these hormones, thereby increasing the lifetime exposure to female hormones (which is associated with increased risk of breast cancer).

IGF-I normally manages the rate at which cells grow and are discarded. However, under unhealthy conditions it becomes more active, stimulating the birth and development of new cells and inhibiting the removal of old cells, stimulating cancer development. Men who eat meat have significantly higher levels of IGF-I compared with vegans [4]. Men with higher than normal blood levels of IGF-1 have 5.1 times the risk of advanced stage prostate cancer [50].

In addition, sulphur-containing amino acids from animal protein lower blood pH which suppresses production of 1,25(OH)2 vitamin D [1,25(OH)2D], the biologically active form of vitamin D [107]. Vitamin D deficiency has been implicated as a risk factor in various cancers, including prostate cancer [107], though one case–control study found that both low and high levels of 25(OH)vitamin D_3 were associated with prostate cancer [256]. Vitamin D is discussed in Chap. 4.

Principle 5: Incorporate Healthy Dairy Products

Approximately 64% of the total calories from whole cow's milk are from fat [42]. Thus, diets high in dairy foods may contribute substantially to the overall amount of fats in the diet. This may be relevant if a person is overweight or obese. In relation to whether dairy foods might be associated with cancer, the evidence is mixed.

Animal Research

Studies in rats have found that increased intakes of casein, a protein in milk, was associated with promotion of development of mammary cancer, operating through a network of reactions, and also via the same female hormone system that operates in humans. Rat and mice studies also showed that diets high in casein promote liver cancer [42].

Link Between Dairy and Prostate Cancer

The World Cancer Research Fund and American Institute for Cancer Research Second Expert Report found that diets high in calcium are a probable cause of prostate cancer, and there is 'limited evidence' that high milk and dairy consumption can cause prostate cancer. There is 'limited evidence' that cheese consumption is associated with colorectal cancer [276].

Systematic reviews have also found evidence of an association between dairy products and prostate cancer [276]. One review found that men with the highest dairy consumption had approximately twice the risk of prostate cancer, and four times the risk of metastatic or fatal prostate cancer compared with those consuming low amounts [49]. The potential mechanisms underlying the association with dairy and prostate cancer may include IGF-I which increases with intake of animal-based foods such as meat and dairy. In addition, milk and other dairy foods have animal protein and large amounts of calcium which can suppress the production of 1,25 Vitamin D (which plays a role in prevention of cancer) [42].

Colorectal Cancer and Dairy

The World Cancer Research Fund and American Institute for Cancer Research Second Expert Report found 'limited evidence' that cheese consumption is associated with colorectal cancer and that milk 'probably protects against colorectal cancer' (it also found there is 'limited evidence' that it protects against bladder cancer) [276].

Breast Cancer and Dairy Foods

An earlier meta-analysis did not find an association between intake of dairy foods and breast cancer [177]. A more recent meta-analysis found that dairy consumption was inversely associated with risk of developing breast cancer and that the type of dairy was important—subgroup analysis demonstrated that yoghurt and low-fat dairy significantly reduced the risk, whilst other sources of dairy did not [287].

Benefits Associated with Different Types of Milk

Cows eliminate toxic substances via fat. Therefore, one might postulate benefits of low-fat milk. Organic milk will not have associated toxicity derived from pesticides and other chemicals used to spray grass and foods that the cows feed on. Also, there

is increasing evidence of an association between A1 beta-casein, a protein produced by the majority of cows of European origin, and milk intolerance. Digestion of bovine A1 beta-casein but not A2 beta-casein has been found to lead to activation of μ-opioid receptors in the gastrointestinal tract and body and rodent studies have shown that it significantly increases an inflammatory marker myeloperoxidase [197].

Good Sources of Dairy

There are good sources of dairy including natural yoghurt and kefir which contains a range of probiotics that are beneficial to the gut microbiome. Thus, it is useful to incorporate some of the good sources of dairy like yoghurt and kefir, in particular in patients who have been given antibiotics. Most of the commercial yoghurts and other fermented dairy products are heated to sterilise them. Hence, it is important to select a non-sterilised product to obtain maximum benefit. Probiotics will be discussed in detail under **Principle 12**: Eat For Your Gut Microbiome.

Principle 6: Reduce Overall Consumption of (Unhealthy) Fats

This section will discuss overall fat intake in diet, whilst the section following this will hone in on different kinds of fats and oils.

Expert Panel Findings on Fat Intake and Cancer

The World Cancer Research Fund and American Institute of Cancer Research Second Expert Report found that there is 'limited evidence' that total fat intake is a cause of postmenopausal breast cancer, and that total fat intake and butter consumption (separately) are causes of lung cancer (though it stressed that the main cause of lung cancer is still tobacco). They also found there was a limited amount of fairly consistent evidence that animal fat consumption is a cause of colorectal cancer [276].

Population Studies of Fat Consumption and Interventions of Lowered Fat Intake

Epidemiological research indicates that high fat intake is associated with several chronic diseases including cancer. Countries with a higher intake of fat, in particular

animal fats, have a higher rates of breast cancer [42, 46, 110, 220, 260]. Nearly 30 years ago, the 1988 Surgeon General's Report on Nutrition and Health stated that comparisons between populations indicated death rates for cancers of the breast, prostate and colon were directly proportional to estimated dietary fat intakes [260].

However, there have been some conflicting findings in several large intervention studies, with some suggesting that lowering fat intake is associated with decreased breast cancer risk [52] and others suggesting it isn't [59, 104, 208]. The Women's Intervention Nutrition (WIN) Study in 2437 women with breast cancer found that after 60 months, those in the low-fat diet had a significantly lower disease recurrence (9.8%) than those in the control group (12.4% women) corresponding to a 24% reduced risk [52]. The Women's Health Initiative Study found a non-significant reduction (9%) in breast cancer incidence associated with a low-fat diet in postmenopausal women over 8 years follow-up (it just failed to reach statistical significance thus the result still may be due to chance) [208] and no significant reduction in risk of invasive colorectal cancer [28]. Research has also found that when overweight/obese postmenopausal women were placed on a very low-fat, high-fibre diet for 2 weeks, there was a significant reduction in serum insulin and IGF-1, and in vitro growth of breast cancer several cell lines was reduced and apoptosis increased [22]. A low-fat, high-fibre diet was associated with lower serum bioavailable estradiol concentration in women diagnosed with breast cancer [219]. These studies suggest that low-fat/high-fibre diets, at the level of physiology might play a positive role.

Problems with Research Methodology

Contrary to findings of others, there have been other studies in women with breast cancer including the large Nurses' Health Study that did not find any association between lowering fat intake and breast cancer [59]. This study has been criticised by Campbell and Campbell [42] who explain that in this study population, there was a very *low* correlation between animal protein and total fat intake (being a typical American diet), and whilst there was variation within the cohort of percentage of calories from fat in their diet, the nurses nearly all ate a diet that was rich in animal foods. Thus, they explain, the Nurses' Study cohort was not adopting the diets shown in the China Study or other international studies to be associated with low breast cancer rates [42], that is diets low in animal-based foods. In the China Study and other international correlation studies, the correlation between fat intake and animal protein intake has been high. The China Study of rural Chinese found that when dietary fat was reduced from 24% to 6%, risk of breast cancer was lowered. However, the authors argued that this might be a reflection of an association between animal-based foods and breast cancer [42].

There's another point to be made about the study methodology involved population studies—unless they look at the types of fats involved, it's difficult to make

a comment about the impact of low- or high-fat diets—some fats are very good for the body, others are not. A high fish fat diet, for example, has been found to reduce colorectal cancer recurrence [239]. Avocado is another food that contains beneficial fats. Even if a diet was low in fat, if these were bad fats, then conceivably it might not confer any protection against breast cancer or other cancers. Not all oils and fats are created equal.

Principle 7: Consume Healthy Fats and Oils and Avoid Unhealthy Ones

Fats and oils are the most energy-dense components of diets. Dietary fats sources include animal products, including meat, milk and other dairy foods, as well as plants, including nuts and seeds. Meat, milk and dairy are the major sources of fat in most high-income countries [276]. A number of oils and fats are beneficial for the body, whilst some have been linked with disease. High levels of trans-fatty acids have also been associated with coronary heart disease [276] and raised levels of CRP [167], a marker of inflammation, and because of this should definitely be avoided.

Dietary fat is mostly made up of triglycerides, three fatty acid molecules attached to a glycerol backbone. These fatty acids are either 'saturated' or 'unsaturated'. Unsaturated fats are typically divided into monounsaturated fatty acids (MUFAs) and polyunsaturated fatty acids (PUFAs). For further information see Table 3.6.

Table 3.6 Unsaturated and saturated fats

• Unsaturated fatty acids may be monounsaturated (they have one double bond) or polyunsaturated (≥ 2 double bonds)
• Where the first double bond is located along the carbon chain is denoted by an 'n'. Linoleic acid is '$n-6$' (also known as Omega-6 fatty acids) and alpha-linolenic acid is '$n-3$' (also known as Omega-3 fatty acids)
• Saturated fats tend to be solid at room temperature whilst unsaturated fats are liquids i.e. oils
• When unsaturated fatty acids in oils and marine sources undergo partial hydrogenation, they are transformed into trans-fatty acids whilst if they undergo complete hydrogenation, they are transformed into saturated fatty acids
• Conversion into saturated fatty acids extends the shelf life of the unsaturated oils that would, under normal conditions, potentially go rancid
• Trans-fatty acids have been linked with cardiovascular disease; however, the effect on cancer is unknown [276]

Omega 3 and Omega 6 PUFAs

Polyunsaturated fatty acids (PUFAs) include Omega 3 ($n-3$ PUFAs), Omega 6 ($n-6$ PUFAs) and Omega 9 ($n-9$ PUFAs). There are both short-chain forms of $n-3$ PUFAs (alpha-linolenic acid, the only Omega 3 source found in plants) and long chain forms (eicosapentaenoic acid, EPA and docosahexanoic acid, DHA). The best sources of $n-3$ PUFAs are fish oils about which quite a lot is known. The Japanese have a diet that is high in fish that contain healthy $n-3$ PUFAs and this contributes to them having one of the highest life expectancies.

Omega 6 is divided into a short-chain form, linoleic acid, which is the most prevalent PUFA in western diets, and the longer chain form, arachidonic acid (AA). Both $n-3$ and $n-6$ PUFAs are essential fatty acids that need to be taken into our bodies via diet.

n − 3 PUFAs and reduced risk of cancer

The $n-3$ PUFAs are particularly important as they have been shown to decrease risk of particular cancers including breast, prostate, colorectal cancer and adenocarcinoma [74, 89, 145, 259]. The EPIC study, a prospective study of 478,000 men and women in Europe, found that fish intake was inversely associated with risk of colorectal cancer [189], and laboratory studies have found these can reduce the progression of colorectal cancer [259]. Another study found that intake of EPA was associated with decreased risk of ER + PR + breast cancer [145] and that n-6 PUFA intake was positively associated with development of ER+ PR+ tumors (which are the majority of breast cancers) [145]. Omega-3 fatty acids are likely to exert anti-cancer effects by impacting several different pathways associated with cancer pathogenesis including cell proliferation, cell survival (including promoting apoptosis), angiogenesis, inflammation, metastasis and epigenetic abnormalities [136].

The importance of the ratio of n − 6 to n − 3 PUFAs

The $n-6$ PUFAs also play an important role in the body; however, the problem is that they are also pro-inflammatory. The ratio of $n-6$ PUFAs to $n-3$ PUFAs is very important: high levels of $n-6$ PUFAs or a high $n-6$ to $n-3$ PUFA ratio promotes inflammatory conditions and diseases such as cancer and cardiovascular disease, whereas increased levels of $n-3$ PUFAs or a low $n-6$: $n-3$ PUFA ratio is suppressive for such conditions [235]. The ratio of $n-6$ to $n-3$ PUFAs 3 in western diets is somewhere between 10:1 and 25:1 [273, 235, 236], whereas several sources suggest that humans evolved on a diet where the ratio of these two fatty acids was closer to 1:1 [235]. This may be due to the move away from animal fats towards polyunsaturated vegetable oils and margarines [214, 273]. Western diets are therefore excessive in the amount of $n-6$ and deficient in $n-3$ PUFAs. Recent research has demonstrated benefits of lowering the $n-6$ to $n-3$ PUFA ratio which was found to be associated with decreased risk of COX-dependent adenocarcinoma [74]. Sources of $n-3$ and $n-6$ PUFAs are set out in Table 3.7.

For further information about $n-3$ and $n-6$ PUFAs, refer to the Additional Reading section of this chapter.

Table 3.7 Examples of sources of $n-3$ and $n-6$ PUFAs

Short-chain $n-3$ (alpha-linolenic acid) sources	Long chain $n-3$ (EPA, DHA) sources	$n-6$ linoleic acid sources	$n-6$ arachidonic acid sources
Flaxseed oil, walnuts (black, English and Persian), chia seeds, dried butternuts, beechnuts, green and raw soybeans, dry soybeans (lesser amount than the green, raw ones), oats/germ, other nuts (hickory, almond, pecans, mixed nuts)	EPA: Fish, fish oils, marine sources DHA: Fish, fish oils, specialty egg/dairy products Fish sources containing DHA plus EPA include: Atlantic salmon, raw European anchovy, Atlantic herring, mackerel, trout	Vegetable oils: corn, sunflower, safflower, soybean, canola, peanuts Animal meats	Animal sources only: liver, egg yolks, animal meats and seafood

Based on data from Mercola [174], Wilkinson [273], DHA/EPA Omega 3 Institute [73]

Patient Advice
On a more practical note it is far too difficult for the patient to try to work out ratios of $n-3$: $n-6$ oils. It's far easier simply to advise them to emphasise the sources of Omega 3 fatty acids such as fatty fish (salmon and others), which can be added to their diet.

Flaxseeds and Lignans

Flaxseeds are a good source of $n-3$ PUFAs; however, there is a difference between flaxseeds and flaxseed oil (as there is between sunflower seeds and sunflower oil). The oil is highly unstable whereas the seeds are not. Importantly, as well as being a good source of $n-3$ PUFAs, specifically alpha-linolenic acid, flaxseeds also contain important lignans which have anti-cancer properties [273].

Lignans are compounds found in most fibre-rich plants including grains (wheat, barley, and oats), legumes (e.g. beans, lentils, and soybeans), vegetables (e.g. garlic, asparagus, broccoli, carrots, soybean), seeds (sesame, pumpkin) and some berries [251]. The major lignan in flaxseed is called secoisolariciresinol diglucoside (SDG) which is converted in the large intestine to active mammalian lignans, enterodiol, and entero-lactone. There is evidence that these active lignans are able to reduce the growth of tumors, in particular those that are hormone-sensitive (breast, endometrium, and prostate) and skin cancer [251].

Hint: Fish Versus Flaxseeds as Sources of $n-3$ PUFAs
Flaxseed mostly contains alpha-linolenic acid (ALA), and the body needs to convert this to the essential fatty acids, EPA and DHA. However, it is estimated that only 5–10% of ALA is converted to EPA and only 2–5% if converted to DHA. In contrast, fish such as salmon and krill are direct sources of EPA and DHA. Fish also contain a lot of other beneficial nutrients including protein, iodine, selenium, vitamin D and other vitamins and minerals depending on the species of fish [112]. Thus, in terms of sources of DHA and EPA, it is best to consume fish about which we know quite a lot.

Olive Oil

Olive oil is a key feature of the Mediterranean Diet which has been found to be associated with lower risk of cardiovascular disease and cancer, as discussed at the beginning of this chapter. Epidemiological studies have found that consumption of virgin olive oil is associated with reduced cardiovascular disease [221], and atherosclerosis [146]. A systematic review found that olive oil intake was associated with reduced risk of cancers of the upper digestive and respiratory tracts and breast cancer, and possibly colorectal cancer [201].

The major phenolic compounds including simple phenols (hydroxytyrosol, tyrosol), secoiridoids (oleuropein) and lignans in olive oil have antioxidant capacity, and are able to scavenge free radicals and protect against peroxidation [196]. Experiments in mice have shown that Extra Virgin Olive oil has strong analgesic, anti-inflammatory effects, and anti-cancer effects, inhibiting the growth of colon tumors [94]. Rat studies have also found that dietary olive oil may prevent colon carcinogenesis, the effects which partly may be via modulation of arachidonic acid metabolism and local PGE2 synthesis [23].

It is of interest that the olive tree can survive up to 2000 years, and it is thought that this is due to the protective chemicals that the trees can produce. It would appear that some of these protective chemicals may also protect humans who consume the olives and other components of the plant.

Coconuts and Coconut Oil

In the past, because coconut oil contains saturated fat it has been denigrated along with other saturated fats. However, in more recent times there has been an increased interest in the protective capabilities of coconut. The various parts of the coconut, including the coconut kernel and water and oil, have a range of medicinal properties

including anti-bacterial, anti-fungal, anti-viral, anti-parasitic, antioxidant, hypoglycemic, anti-atherogenic, anti-thrombotic and immunostimulatory effects [65].

Canola Oil and Other Vegetable Oils

In general, vegetable oils should be avoided in favour of healthier oils including olive oils, avocado oils and coconut oil. The higher use of vegetable oils such as sunflower oils and spreads which are rich in $n-6$ PUFAs has dramatically shifted the ratio of $n-6$ PUFAs to $n-3$ PUFAs [234]. This has shifted the balance of eicosanoids synthesised from DHA and EPA (produced from $n-3$ PUFAs) to favour eicosanoids derived from arachidonic acid (synthesised from $n-6$ PUFAs); arachidonic acid leads to the production of leukotrienes, prostaglandins and thromboxanes, including platelet activating factor (PAF). [214]. This imbalance leads to a pro-inflammatory state.

Canola oil is produced from the rapeseed plant. Rapeseed oil is a monounsaturated oil with a high erucic acid content, a fatty acid associated with Heshan's Disease which causes fibrotic lesions in the heart. A large amount of canola oil is now genetically modified, and the process used to modify the rapeseed plant produces canola oil with less erucic acid and more oleic acid. The safety of long-term ingestion of the small quantities of erucic acid in canola oil has not been established. In addition, it undergoes a deodorization process that turns Omega-3's into trans-fatty acids. Consequently, there have been concerns about increased cancer risks due to the hydrogenation process, blood platelet abnormalities, free-radical damage and retardation of normal growth (it is illegal to use in infant formulas) [79].

In general, oils from trees appear to be protective whereas oils from other types of plants do not.

Nuts

Nuts have been found to confer health benefits, discussed earlier. A 2013 study found that a handful of mixed nuts each day will increase longevity by 20% [20]. A study of over 34,192 Seventh Day Adventists found that those who ate nuts ≥ 5 times/week had a significantly (50% less) reduced risk of fatal and non-fatal ischaemic heart disease compared to those who ate nuts <1 time/week [102]. Most nuts contain mostly Omega-6 fatty acids so they should be balanced with Omega-3 oils [273]. Remember, Omega-6 fatty acids are necessary in the diet, it's the ratio to Omega-3's that needs to be right.

Take Home Messages About Fats

Take Home Messages About Fats

1. Limit intake of foods high in saturated fat (some of which often also contain refined sugar) such as many biscuits, cakes, pastries, pies, processed meats, commercial burgers, pizza, fried foods, potato chips, crisps and other savoury snacks
2. Good oils to add to diet include olive oil, avocado, coconut
3. Avoid fried foods, canola oil and other vegetable oils including safflower and sunflower
4. Evidence suggests that fish fats are the most protective
5. Remember to add oils before serving vegetables (so that you are getting some good oils that have not been altered by heat)
6. Add a handful of nuts to diet daily—include walnuts which contain Omega-3 fatty acids and brazil nuts which contain selenium
7. Cook with oils that have a high smoke point and are healthy, e.g. olive oil, coconut oil, sesame oil, grape seed oil, rice bran oil or macadamia nut oil.

Principle 8: Keep Hydrated But Choose Your Drinks Wisely

In this section, we will look at some popular beverages, including coffee, green and black tea, water, soy and alcohol. But first, a quick note about the temperature of drinks and what the current evidence indicates.

Some Like It Hot (But It May Not Be Good for You)

The 2016 International Agency for Research on Cancer (IARC) review of coffee, mate and very hot beverages concluded that there is 'limited evidence' in humans for the carcinogenicity of drinking very hot beverages in relation to oesophageal cancer [166]. This conclusion was based on studies of drinking mate (South American drink), tea and other very hot beverages. Another study similarly found an association between increased temperature and increased risk of oesophageal cancer [132]. Thus, it would be prudent to advise patients to drink their beverages at slightly lower temperatures and avoid hot or very hot temperatures.

Coffee

Over recent years, there is increasing evidence that coffee may be beneficial for health and that it is not a risk for cancer that it was once thought it could be. In fact, it may even be protective against some cancers. Drinking coffee enhances social communication, giving it a very important added benefit in terms of health.

Classification in relation to potential carcinogenicity

There have been over 500 epidemiologic studies in Japan, Europe and America investigating whether there is an association between coffee drinking and risk of developing a range of cancers [57]. The International Agency for Research on Cancer (IARC) reviewed the scientific evidence in relation to coffee and carcinogenicity. In its previous review in 1991, the IARC classified coffee as 'possibly carcinogenic to humans (Group 2B)'. That classification has now changed—it has been classified as 'unclassifiable as to its carcinogenicity to humans (Group 3)' [166]. The 2016 IARC review of the literature found no consistent association between coffee consumption and bladder cancer, and no association with pancreas or prostate cancer. Either no association or a modest inverse association was found between coffee consumption and female breast cancer, and there was evidence of an inverse relationship for liver and endometrial cancers. The evidence in relation to a range of other cancers, however, was found to be inadequate.

> '*Caffeine intakes from all sources up to 400 mg per day (about 5.7 mg/kg bw per day for a 70-kg adult) consumed throughout the day do not give rise to safety concerns for healthy adults in the general population, except pregnant women (see below). No health concerns in relation to acute toxicity, bone status, cardiovascular health, cancer risk or male fertility have been raised by other bodies in previous assessments for this level of habitual caffeine consumption and no new data have become available on these or other clinical outcomes which could justify modifying these conclusions*' **European Food Safety Authority 2015** ([84], p. 74).

Evidence of a protective effect of coffee against cancer

When looking at individual studies, there is evidence that coffee may be protective against particular cancers. Research has found that coffee consumption is associated with a reduced risk of a range of cancers including the following:

- colorectal [105, 160, 228]
- pancreatic [76, 284]
- liver cancer [19, 37, 224], as well progression to liver cancer in Hepatitis B carriers [159] and progression of liver cancer in those with Hepatitis C [99]
- oral cavity and pharynx [257, 284, 290]
- glioma [176]
- oesophageal [284, 291].

Coffee and breast cancer

The research conclusions are mixed for breast cancer [57]. In women with BRCA1 and BRCA2 mutations, it seems that coffee may be protective against breast cancer [188]. In postmenopausal women, coffee consumption has been found in several studies to reduce risk of breast cancer also [246, 161]. However, a recent meta-analysis found no significant association between coffee consumption and reduced risk of breast cancer except in the case of oestrogen receptor-negative women where an inverse relationship was found [163] and another meta-analysis analysis found a weak relationship between coffee consumption and increased risk [134]. For stomach, lung cancer and bladder cancer, the research is inconclusive. A detailed summary of research on coffee and its effects on health can be found at the Institute for Scientific Information on Coffee [57].

Coffee and co-morbidities

Since cancer sufferers often have or can develop co-morbidities, it is worth noting that there is also some evidence that coffee is protective against diabetes [261] and can confer neuroprotection in Parkinson's Disease [207].

Tea

Tea has been found to have many positive health benefits including lowering cholesterol, and preventing age-related memory loss and has anti-cancer and anti-inflammatory properties.

There are several compounds in tea including polyphenols, alkaloids (caffeine, theophylline, theobromine), chlorophyll, amino acids, carbohydrates, proteins, fluoride, aluminium, minerals, volatile organic compounds and trace elements. The health benefits of tea are thought to be due to the polyphenols, which include the catechins. The most abundant catechin in green tea is epigallocatechin-3-gallate (EGCG); others include Epigallocatechin (EGC), Epicatechin-3-gallate (ECG) and Epicatechin (EC). Black tea also has these catechins; however, the concentrations of these are much lower than in green tea [183].

Anti-cancer properties of tea

There is evidence from animal studies and epidemiologic studies of humans that suggest that tea may have anti-cancer properties. Animal studies have demonstrated that tea and its constituents are able to inhibit cancers of the skin, lung, oral cavity, oesophagus, liver, stomach, prostate and others [155]. Results of over 50 epidemiologic studies of the association between tea consumption and risk of cancer published since 2006 have been variable; however, some have found an association between tea intake and reduced risk of cancers of the colon, breast, ovary, prostate and lung. Inconsistency of research results may be due to lifestyle factors, smoking, alcohol consumption, tea preparation methods and others [183]. Two randomised

controlled trials have found green tea consumption was associated with a decrease in a marker of oxidative DNA damage that may be a predictor for increased cancer risk [111, 168].

Mechanisms of action of tea

The exact mechanisms by which green tea may help prevent cancer have not been established. However, the main polyphenols in green tea and the theaflavins and thearubigins in black teas are protective plant chemicals and may protect cells against DNA damage [117]. Tea polyphenols can inhibit tumor formation and induce apoptosis [155], and tea catechins can inhibit angiogenesis and tumor cell invasiveness [288]. Other mechanisms of action of green and black tea include anti-mutagenic, anti-proliferative and anti-neoplastic activity. For more information about green and black tea, see the Additional Reading section at the end of the chapter.

Key Point

- Green tea has more protective chemicals and in higher amounts than black tea and is therefore more protective; however, black tea still has some beneficial actions.

Soy

Soy is widely consumed in Asia in a variety of forms, including tofu, dried or green or fermented soybeans, miso (fermented soy bean paste), soy milk and others. There is some controversy in the literature about whether soy is good or bad for health, particularly in western countries. There seems to be a fear that soy, being a phytoestrogen, is somehow dangerous to women with oestrogen-receptive-positive cancers. However, these phytochemicals are often significantly altered (into many different metabolites) by the gut flora. Much more research into the potential benefits (or otherwise) of these metabolites is necessary before any definitive statements can be made.

Asian women have a lower rate of breast cancer than in western countries [6]. Higher intake of soy during childhood and adulthood in Asian-American women was found to be associated with a reduced risk of breast cancer [280]. A meta-analysis found that in Asians, risk of breast cancer decreased with increasing intake of soy, whilst in the relatively low soy-consuming Western populations, soy intake was unrelated to breast cancer risk [282]. Another meta-analysis of 18 epidemiologic studies from 1978 to 2004 that examined soy exposure and breast cancer risk found that when the results of all women were considered, high soy intake was modestly associated with a reduced risk of breast cancer (OR 0.86, 14% reduction) but there was no significant association when only women from Asian countries were analysed [255]. This may have been due to the low baseline of breast cancer in Asia to begin with.

Soy contains isoflavones, phytoestrogens that are thought to reduce risk of breast cancer, with Genistein, Daidzein and their glucosides being the main ones. Several in vitro studies and animal studies have demonstrated that soy or isoflavones have anti-cancer effects on hormone-related cancers, and there may be several mechanisms involved including oestrogenic and anti-oestrogenic activities [195, 175].

Water

The recommended intake of water is 6–8 glasses per day; however, this can vary depending on illness, exercise, spending time in the heat and other factors. A good rule of thumb is to sip water or healthy, low-caffeinated green or herbal teas during the day and listen to your body to regulate intake and adjust when needed. Clinicians can advise patients to check the color of their urine as an indicator of hydration—darker urine can indicate the need for better hydration.

Much of the water supply in countries like Australia and the US has additives such as chlorine, fluoride and, other contaminants such as trihalomethanes. Serious contaminants can also make their way into drinking water, including chemicals used to spray crops, industrial pollutants and chemicals leached out of plastic pipes used to carry water.

Coal-fired power plants are problematic. Relatively large amounts of particulate and oxidised mercury are released from these power plants and they are rapidly deposited locally [222]. Bodies of water nearby are expected to receive greater atmospheric deposition of mercury than those further away [141, 222]. One study found that contrary to what would be expected, the mercury level in fish closer to coal power plants was lower than fish in lakes further away [222]. However, this finding was found to be associated with selenium—levels of selenium were found to be much higher in lakes closer to coal power plants, and selenium antagonizes mercury. The study also concluded that water quality characteristics such as pH, sulphate, and DOC all play important roles in mercury accumulation in water systems and fish tissue [222].

Fluoride in water

There is evidence that contaminants in water including fluoride may be toxic to the body and associated with a range of diseases including cancer [158]. This is, of course very controversial, but with such large vested interests involved, this would hardly be surprising.

Biochemist Dr. John Yiamouyiannis spent several years researching the toxicity of fluoride and found that fluoride is cumulative, and that it damages the immune system, poisons more than 100 enzymes, increases risk of cancer, and increases the risk of autoimmune diseases, amongst other things [158]. Dr. Dean Burke, former head of the Cytochemistry Section of the U.S. National Cancer Institute and Dr. John Yiamouyiannis created quite a stir in the 1970s when they testified before the US Congress that there was a greater rate of cancer in ten fluoridated US cities compared with ten non-fluoridated ones [283].

Epidemiological studies have suggested an association between fluoridation of water and osteosarcoma as far back as 1955 [61], including a matched case–control study in young boys that found exposure to fluoride in their 6th to 8th years was associated with a five to sevenfold increase in risk of contracting osteosarcoma by age twenty [25]. Studies in male rats have also demonstrated a significant dose-related increase in risk of osteosarcoma [185]. The vast majority of western European countries do not fluoridate their water [97].

Chlorine in water

Fluoride is not the only villain: exposure to chlorine in water (chlorination disinfection by-products), including from bathing and swimming, has also been linked to bladder cancer [172, 266, 124] and possibly other cancers including brain [44] and colorectal cancer [81], and other chemicals including arsenic have also been implicated in several cancers also [170].

Water filters

Where possible, it is advisable that water is filtered to remove as many impurities as possible, and alkalinise the water. Filtered water also tastes better. Reverse osmosis filters are able to remove the majority of fluoride in town water, and there are a variety of options including whole house water filtration systems, smaller units that filter via the water taps, and benchtop units. Of course, the cost varies considerably. Bottled water, whilst handy when travelling, may not be a great environmental choice if used on a daily basis. Australians are particularly high consumers of bottled water, which is curious given their relatively clean water supply. However, this may not be so much about health concerns as savvy marketing.

Alcohol

There is some controversy about whether consuming alcohol can confer benefits or the opposite for health. For years it was believed that moderate consumption of alcohol had a cardio-protective effect. In more recent times, however, it has been found that there is convincing evidence that alcohol can cause cancer of the oropharynx, larynx, oesophagus, liver, colon, rectum and breast [62, 276] and probably also pancreatic cancer [258]. It is estimated that worldwide, alcohol-attributable cancers at these sites constitute 5.8% of all cancer-related deaths [62]. There is also growing evidence to implicate alcohol in development of skin, prostate and pancreatic cancer [116, 231, 223]. The risk of cancer has been found to increase with increasing alcohol consumption on a regular basis.

For women, increased alcohol consumption has found to be (statistically) significantly associated with increased risk of cancer of the oropharynx (increased risk per 10 g/day of 29%), oesophagus (22%), larynx (44%), rectum (10%), liver (24%), breast (12%) and total cancer (6%). The trends were similar for those who only drank wine compared to those who drank other types of alcohol [5].

Some of the evidence in relation to the association between alcohol and cancer risk is set out in Table 3.8.

Table 3.8 Evidence of association between cancer and alcohol

Colorectal cancer
• A meta-analysis of 61 studies found that consuming more than one drink per day is associated with increased colorectal cancer risk; risk increased with amount of alcohol consumed daily [91] • A meta-analysis found a J-shaped relationship between alcohol consumption and colorectal cancer, providing evidence for a statistically significant association with heavy ($\geq$50 g/day), though not light or moderate, alcohol drinking and colorectal cancer mortality [39] • A meta-analysis of 57 studies found that people who regularly drank around 3.5 drinks daily had 1.5 times the risk of developing colorectal cancer compared to occasional drinkers or non-drinkers [91]
Breast cancer
• A meta-analysis of 53 studies found that women who drank more than 45 g alcohol/day had almost 1.5 times the risk of developing breast cancer compared to non-drinkers (Relative Risk 1.46), and in those who consumed 35–44 g alcohol/day, there was a 32% increased risk of breast cancer (Relative Risk 1.32). For every 10 g alcohol consumed per day, there was a 7% increase in risk of breast cancer [113] • Other meta-analysis studies have supported the contention that alcohol consumption is associated with increased breast cancer risk [142] • The Collaborative Breast Cancer Study, a population-based study found that moderate alcohol intake before breast cancer diagnosis was associated with lower overall breast cancer mortality (3–6 drinks/week vs non-drinkers: HR 0.85); however, they found no association with alcohol intake after diagnosis [186] • A prospective Danish cohort study found an increased risk of recurrence with higher alcohol consumption (>2 units/day vs. $\leq$1 unit/day: HR 1.65) but also found that average alcohol intake was greater after breast cancer diagnosis compared to before [123] • The After Breast Cancer Pooling Project which is the largest and longest study so far to assess recurrence found that overall increased levels of alcohol were not associated with recurrence or overall survival, but there was an increased risk of recurrence in postmenopausal women who regularly consumed alcohol ($\geq$6.0 g/day) (HR, 1.19; 95% CI, 1.01–1.40) [152]
Head and neck cancer
The NIH-AARP Diet and Health Study found mixed results in relation to the association between alcohol consumption and risk of head and neck cancer: • There was evidence of a dose–response relationship between alcohol consumption and risk of head and neck cancer: women and men who consumed >3 drinks per day has 2.5 and 1.5 times the risk of cancer (Hazard Ratios 2.5 and 1.48 respectively) • Consumption of up to one standard alcoholic drink per day was associated with lower risk of head/neck cancer compared to non-drinkers [100]

Mechanisms of action

The mechanisms by which alcohol may contribute to cancer include the following:

- Metabolism of ethanol in alcohol produces acetaldehyde which is a carcinogen that can damage cellular DNA and proteins. The International Agency for Research on Cancer (IARC) has listed acetaldehyde as a Group 1 Carcinogen. The metabolism of acetaldehyde on the other hand produces acetic acid, an extremely important communications molecule for the immune system.
- Generates reactive oxygen species which damage DNA, proteins and fats.

- Impairs body's ability to absorb nutrients which are associated with increased risk of cancer (e.g. Vitamins A, C, E, folate, carotenoids).
- Raises oestrogen levels (which are implicated in higher risk of breast cancer) [171].
- Ethanol is hypothesised to play a role in breast cancer development by down-regulating the tumor suppressor gene BRAC1, causing increased transcriptional activity of ERα (key oestrogen receptor) which then leads to increased cell proliferation and increased chance of genetic damage [171].

Some evidence of benefits of wine

There is research that suggests some benefits associated with one of the components of red wine, resveratrol (Malbec and Pinot Noir varieties contain the most). Laboratory research indicates that resveratrol has several anti-cancer properties including being anti-inflammatory, antioxidant, an immune system modulator, being able to block cancer cell proliferation and being able to sensitise cancer cells to chemotherapy [273]. It also has antibiotic and anti-fungal properties [273].

Key Point
Resveratrol can be obtained by eating fruits that contain it such as raspberries and red grapes, or by taking a resveratrol supplement, rather than drinking alcohol.

A recent study in female patients with non-Hodgkinson's lymphoma found that pre-diagnostic wine consumption reduced the risk of death and relapse in women. The study found that women who drank wine had better overall survival than women who had never drunk wine. In those with diffuse large B cell lymphoma (DLBCL), those who consumed wine for more than 25 years had a significantly reduced risk of death and risk of relapse, secondary cancer or death (64 and 62% reduction respectively). However, DLBCL patients who started drinking liquor before the age of 21 had a significantly increased risk of death and increased risk of relapse, secondary cancer or death compared to those who were 'never drinkers' [114].

Recommendations on alcohol consumption in relation to cancer

The general advice given in dietary guidelines, such as recommendations from the World Cancer Research Fund and American Institute for Cancer Research Second Expert Report is that, based on evidence in association with cancer, no alcohol should be consumed [276]. However, this report also stated that on the basis that there is some evidence of a cardio-protective effect, if alcohol is to be consumed, men should limit their consumption to no more than two drinks per day and women should limit theirs to one drink per day [276]. Red wine is a healthier choice than sweet white wine.

The U.K. Chief Medical Officers' Low Risk Drinking Guidelines 2016 (revised from the previous one in 1995) advises that the risks of particular cancers '*starts from any level of regular drinking and then rise with the amounts of alcohol being*

drunk'. It also states that '*there is no level of regular drinking that can be considered as completely safe in relation to some cancers. People can reduce these risks by drinking less than the guidelines or by not drinking at all*' [258].

Many alcoholic and mixer drinks are high in sugar and kilojoules and may contribute to weight gain, so this should be remembered in relation to patients who are already overweight or obese.

Juices

Commercially available fruit juices, where fibre has been removed, are high-sugar foods which cause a sharp increase in sugar in the bloodstream with consequent insulin spike [273]. Juicing of fruits and vegetables is popular and has the advantage of combining a wide range of vegetables including those that may not normally be eaten. If the fibre is filtered out though, the juice should still be a considered high-sugar food. There are machines available which blend the whole fruit including the flesh or pulp, rather than filtering it out, thereby retaining the healthy fibre in the vegetable or fruit. This fibre is useful for healthy bowel function and is essential for the microbiota of the gut.

Eating the whole fruit or vegetable has some distinct advantages. When the whole fruit is eaten, it cannot be consumed so quickly, and it contains fibre, which both delays absorption of sugar and allows a more gradual uptake. In addition, commercially produced fruit juices have lost much of their nutritive value.

There are a few other problems with juicing, including producing doses that are more than are needed, so it is prudent to introduce juicing gradually otherwise it might make the patient feel unwell [273]. Juicing also concentrates the bad parts as well as the good parts, such as the pesticide residues [273]. Thus, it is safer to juice organic vegetables and fruit. It is also better to juice mostly vegetables and add just a small amount of fruit for flavour [273].

Another issue with juicing is the removal of the need for chewing. Chewing is an essential part of the digestive process including the delivery of sufficient quantities of saliva to the food bolus. Also, the pleasure of having the food in the mouth for a longer time and the pleasure of extended periods of taste are reduced with drinking juices.

Soft Drinks

There is not much to be said about soft drinks other than the fact that they provide no nutritional value and are most likely to cause spikes in blood sugar. Consumed on a regular basis, they add to the burden of refined sugars in the body, and a pro-inflammatory condition. They are best avoided. Mineral water and sparkling waters that do not contain added sugars are fine (though excess consumption of

carbonated drinks can lead to abdominal bloating and flatulence). Coating one's red blood cells, protein receptors and cell membrane lipids with sugar is a sure way of wrecking your brain and body.

Principle 9: Avoid Excess Sugar, Artificial Sweeteners and Salt

Excessive sugar in the diet has been linked with many chronic illnesses and contributes to a pro-inflammatory condition within the body, and inflammation is part of the pathogenesis of cancer. High glycidic diets have been found to be associated with increased risk of digestive, endometrial, ovarian and colorectal cancers [11–13, 98]. An increased risk of gastric cancer has been found to be associated with high glycaemic load but not high glycaemic index [14, 157]. Excess refined sugar in diet can lead to weight gain, overweight and obesity, with the attendant increase in risks of diseases such as diabetes and cancer.

High-sugar intake can lead to weight gain and diabetes and these are linked to cancer [273]. When there is insulin resistance, the body compensates by secreting more insulin, and this as well as IGF, can promote tumor growth [285]. Fruit juices contain high amounts of sugar and should be limited. Soft drinks also contain extremely high amounts of sugar and have very little nutritional value, so are best avoided. Excess refined sugar is a feature of a substantial amount of processed foods available in supermarkets and take-away (take-out) foods, as is excessive salt.

Artificial and Natural Sweeteners

Artificial sweeteners can contain dangerous chemical compounds and should also be avoided. Natural sweeteners include Yellowbox honey which has a lower glycaemic index than many other honeys. Manuka honey has been found to have several health benefits.

Salt

The World Cancer Research Fund and American Institute of Cancer Research Second Expert Report states that salt and salt-preserved foods are a probable cause of stomach cancer and recommends avoiding salt-preserved, salted or salty foods, to preserve foods without using salt and limit intake of processed foods that have added salt to ensure that daily intake is less than 6 g (2.4 g sodium) [276]. Excessive salt is also linked to hypertension and increased risk of cardiovascular disease [43].

Principle 10: Avoid Foods Containing Acrylamides

Acrylamide is a chemical used to make polyacrylamide and acrylamide copolymers used as soil conditioners, in wastewater treatment, treatment of drinking water, and in the cosmetic, paper, and textile industries [101, 181]. Acrylamides are also produced by cooking certain foods under conditions of high temperatures (above 120 °C or 248 °F) and low moisture, and can be produced from the amino acid asparagine (found in many vegetables, particularly certain types of potatoes) and reducing sugars such as glucose and fructose, though other pathways may also contribute to their formation [45].

Most acrylamides are formed rapidly during the final phases of baking, frying or grilling of foods rich in carbohydrates such as breakfast cereals, cocoa, coffee, fried potato products (e.g. French fries, potato chips) and bakery products (e.g. biscuits) [45]. Boiling and microwaving are less likely to produce acrylamides than baking, frying or broiling [181]. At high temperatures, longer cooking times can increase acrylamide production [181, 277].

Major contributing foods to acrylamide exposure are:

- fried potato products
- bakery products (biscuits, bread) and
- coffee and solid coffee substitutes [84, 88].

Acrylamides Are Carcinogenic to Humans

Acrylamides have been classified as 'probably carcinogenic to humans' (Group 2A) by the International Agency for Research on Cancer [45] and the European Food Safety Authority 2015 report on acrylamides stated a concern for neoplastic effects based on animal evidence [84], similar to an earlier Joint Food Additive Organisation (FAO) and World Health Organization [277] report on acrylamides [277].

Acrylamides are rapidly absorbed in the body and distributed widely to muscle and all organs. They also make their way into the placenta and breast milk, presenting a significant risk to the unborn child, babies and infants [45]. The concern about the potential for acrylamides to cause cancer is based mainly on the fact that it has been established in animal studies that acrylamides can cause cancer [101, 181]. However, there are several studies in humans that also indicate cause for concern in relation to cancer-causing potential including evidence of an association between acrylamides and significantly higher levels of oestrogen-receptor–positive breast cancer [192], increased risk of postmenopausal endometrial and ovarian cancer,

particularly among never-smokers, but not postmenopausal breast cancer [118] and increased risk (men and women) of renal cancer but not of prostate or bladder cancer [119]. Other potential endpoints for acrylamide toxicity identified from animal studies include neurotoxicity, developmental toxicity and adverse effects on male reproduction [84, 88].

Study of Acrylamide Contamination of Foods:
An Italian study showed that in a sample of 56 breakfast cereals and biscuits, 95.5% of the biscuits and 75% of the breakfast cereals were contaminated, and that 22.7% of biscuits and 33% of breakfast cereals exceeded the values recommended by the European Commission EC 2013/647 (500 μg/kg and 200–400 μg/kg, respectively) [45].

Principle 11: Eat Dark Chocolate (Yes, You Read that Correctly)

For those who love chocolate, research provides a justification on the basis of a range of health benefits to indulge in a couple of pieces of dark chocolate, though of course it is the dark chocolate that is better for you than milk chocolate.

Cocoa, which has a higher content of dark chocolate, contains antioxidant compounds including flavonoids, catechin, epicatechin, proanthocyanidins plus a small amount of fibre. Studies in cells have found that cocoa may have beneficial actions in cancer.

- A study in cells found that high concentrations of cocoa polyphenols extracts have an anti-proliferative effect on prostate cancer cell growth and were able to inhibit growth of metastatic and non-metastatic cell lines [138].
- Another constituent of cocoa, a pentameric procyanidin, has been shown to inhibit the proliferation of human breast cells (this substance has also previously been shown to cause cell cycle arrest in human breast cancer cells) [210].
- When mice were fed for 12 weeks with a high-fat diet supplemented with either a cocoa flavanol extract or a flavanol fraction enriched with monomeric, oligomeric, or polymeric procyanidins, it was found that the oligomer-rich fraction was the most effective in preventing weight gain, impaired glucose tolerance, and insulin resistance [78].

The evidence of health benefits of cocoa and chocolate on the cardiovascular system is growing. Chocolate's benefits include antihypertensive, antioxidant, anti-inflammatory, anti-atherogenic effects, anti-thrombogenic, and an influence on insulin sensitivity [38]. Examples of a diversity of findings about chocolate are set out in Table 3.9.

Table 3.9 Some research findings about chocolate and cocoa

• A systematic review of seven studies (114,009 participants) found that the highest levels of chocolate intake were associated with a 37% reduction in cardiovascular disease and a 29% reduction in stroke compared with the lowest levels [38]
• A small clinical trial has found that mitochondrial structure improved in patients with advanced heart failure and type 2 diabetes after 3 months of treatment with epicatechin-enriched cocoa [248]. This effect on mitochondria might be very relevant if the Metabolic Theory of Cancer is in fact accurate (discussed earlier), and mitochondrial damage is at the root of cancer pathogenesis
• In patients with end-stage renal disease, drinking cocoa flavanols for 30 days was associated partial reversal of endothelial dysfunction, decreased diastolic blood pressure, and acute ingestion of cocoa flavanols mitigated haemodialysis-induced arterial dysfunction (and this effect was sustained throughout the 30 day study) [211]
• An in vitro study that looked at the combination of cocoa extract, fish oil and plant sterols was able to hinder several key steps in the process of atherosclerosis [179]. Lavado cocoa (but not Dutch cocoa) which is high in polyphenols was found to prevent clumping of protein β-amyloid-(Ab) and protect against synaptic defects in mice brains, suggesting that it may be useful in Alzheimer's Disease [271]
• Cacao has been found in animal studies to reduce UV-induced skin wrinkling [144]

Hint: a few squares of dark chocolate half an hour before a meal may help sate the appetite and reduce overeating.

Principle 12: Eat for Your Gut Microbiome

As discussed in Chap. 2, there is increasing evidence of a link between the gut microbiome and cancer. Adequate fibre and resistant starch is important in particular for colon health. Beneficial bacteria within the body assist the digestion of food, produce natural antibiotics, and produce some vitamins. This section will look at fibre, resistant starch, prebiotics and probiotics.

Dietary Fibre

Adequate fibre and resistant starch is needed, in particular for healthy intestinal function. There are both soluble and insoluble forms of fibre.

Dietary fibre is found in vegetables, fruit and pulses (legumes) plus cereals/grains (e.g. wheat, rice, maize (corn), millet, sorghum, barley, oats and rye), roots, tubers and plantains. The protective effect of foods high in dietary fibre may be due to their bulk and relatively low energy density (this may be important in relation to overweight and obesity). The World Cancer Research Fund and American Institute for Cancer Research 2007 Report found convincing evidence that foods such as cereals/grains and peanuts contaminated with aflatoxins are a cause of liver cancer [276]. The Report also concluded that foods containing dietary fibre probably protect against colorectal cancer, and that there is limited evidence to suggest that it may protect against oesophageal cancer.

Dietary Fibre and Colorectal Cancer

The potentially beneficial link between a diet high in fibre and decreased colorectal cancer originated from population-based studies that found differences across countries in colorectal cancer rates [225]. Several case–control studies also found evidence of a lowered risk of colorectal cancer with increased dietary intake of fibre [121, 242, 254], though not all have [249]. However, the evidence in relation to prospective cohort studies and dietary intervention studies of colon adenoma recurrence (which are known precursors to colorectal cancer) has not found as much solid evidence for a protective effect of fibre [3, 148, 225, 249].

Why intervention studies, in general, have not found convincing evidence of a relationship between dietary fibre intake and adenoma or colorectal cancer, particularly when much of the epidemiological evidence and case–control studies have pointed to a protective effect may be due to several factors. These include the multi-stage process of colorectal cancer, plus methodological issues in trials including confounding factors, poor adherence to interventions amongst trial participants and the intention-to-treat analysis design favoured in clinical trials [225]. Poor adherence to clinical trial protocols will dilute results, a fact found when the US Polyp Prevention Trial data was re-analysed. The study originally found no difference between recurrence of colon adenomas at the end of a 4-year study (testing the efficacy of a low-fat, high-fibre and high fruit and vegetable diet), but on re-analysis of the data they found a 35% reduction in the odds of adenoma recurrence in those who were the most adherent participants. Thus, high compliance with a low-fat, high-fibre diet was found to be associated with decreased risk of recurrence of adenoma [225]. This re-analysis highlighted an important point in interpretation of study results—reporting compliance with the study intervention is vital, as is interpretation of the results in relation to compliance.

Rates of colon cancer are known to be much higher in African Americans than in rural South Africans (65 per 100,000 compared to <5 per 100,000), and these higher rates are associated with a diet higher in animal protein and fat and lower in fibre, as well as higher colonic secondary bile acids, lower colonic short-chain fatty acids and higher mucosal proliferative biomarkers of cancer risk. A study was conducted where, for 2 weeks, a cohort from each of these populations swapped diets, under close supervision. The study found reciprocal changes in mucosal biomarkers for cancer risk in each group, as well as in aspects of the microbiota and metabolome that are known to affect cancer risk. In the African American group, secondary bile acid synthesis was suppressed [190].

Certainly, there is some indication from animal experiments of mechanisms by which fibre might prevent tumors. For example, rat experiments have demonstrated that high levels of butyrate obtained following fermentation of soluble dietary fibre was found to inhibit early and late events in colon tumorigenesis by controlling key pathways in cell apoptosis [18].

Fibre and Other Cancers

There is some evidence that fibre may protect against breast cancer [90, 92, 198] and it may be protective against mouth, throat and oesophageal cancers [238]. A recent study found that early adulthood total dietary fibre intake was associated with a significantly lower risk of breast cancer, and that both higher intakes of soluble and insoluble fibre were both associated with lower risk. Higher intake of dietary fibre in adolescence was significantly associated with lower breast cancer risk also [90], underscoring the importance of diet in childhood as well as adulthood. A meta-analysis of 10 prospective studies found a significant inverse relationship between breast cancer risk and dietary fibre intake [77].

How fibre exerts its beneficial effects in breast cancer may be partially due to the fact that high-fibre diets are typically lower in fat, and dietary fat is believed to increase risk of breast cancer [260]. In addition, fibre binding to oestrogen in the digestive tract helps expedite the removal of excess oestrogens [204].

Other Benefits of Fibre

Fibre creates a sense of fullness and thereby helps satiate our appetites [42]. It thus may have some advantages in terms of reducing amount of food consumed and therefore weight control. Contrary to past fears, fibre doesn't appear to interfere with iron absorption. The China Study, mentioned earlier in this chapter, found no evidence of this, despite the average fibre intake being about three times higher in rural China compared to the US. In fact, they found the opposite. Average iron intake in rural Chinese was 34 g/day compared with average American intake of 18 mg/day and it was much more associated with plant-based foods than

animal-based foods. Thus, consuming more plant-based foods and therefore more fibre was associated with greater iron consumption, not less [42].

Resistant Starch

Resistant starch is distinct from dietary fibre, and is the total amount of starch and the products of its degradation that resist digestion in the small intestine. Resistant starch is fermented by the bacteria in the large intestine, producing several benefits:

- Increasing stool bulk
- Promoting a mild laxative effect
- Encouraging growth of healthy bowel bacteria (acts as a prebiotic)
- Producing short-chain fatty acids including butyrate which promote a healthy bowel
- Preventing degradation of the mucous layer of the large intestine, which protects colon cells
- Reducing intestinal pH and the production of harmful secondary bile acids, ammonia and phenols
- Reducing the glycemic response [156]

Resistant starch and colorectal cancer

Resistant starch produces butyrate which has been shown to reverse neoplastic changes in colon cells [93]. Consumption of resistant starch decreases ammonia and other nitrogen-containing compounds [29] which are related to increased colon cancer risk [30].

Animal studies indicate that high-resistant starch diets may prevent colon cancer [215]. An early observational study found a linear correlation between starch intake and reduced risk of colorectal cancer (but not between dietary fibre intake and colorectal cancer) [48]. A study in South Africa found that those consuming high levels of maize porridge containing high levels of retrograded resistant starch and low levels of dietary fibre had significantly lower levels of colorectal cancer in comparison to another population who consumed higher levels of dietary fibre, but lower levels of resistant starch, which may suggest that the fermentation of resistant starch was able to confer protection [2].

Sources of resistant starch

Some sources of resistant starch that contain at least 1 g resistant starch per 100 g as eaten include: grains (e.g. millet, barley, oats), breads (pumpernickel, rye, black, white fibre increased), English-style muffins, some breakfast cereals (e.g. processed bran, low-sugar puffed flakes), bananas (green bananas have a much higher content than ripe), mature legumes and pulses (e.g. soy, lentils, split peas), baked beans and corn bread [156].

Table 3.10 Some sources of prebiotics and probiotics

Sources of prebiotics	Sources of probiotics
Onion, garlic, leek, honey, artichokes, soy, wheat, barley, oats, almonds, pistachios, bananas, skin of apples, beans, seaweed and marine microalgae, asparagus, chicory root, acacia gum, raw chicory root, raw honey, whole grain corn, psyllium husk	Fermented foods such as yoghurt, soured milk products, kefir, fermented vegetables such as sauerkraut and kimchi

Based on data from Landon et al. [156], de Jesus Raposo et al. [66], Dr. Axe [80], International Food Information Foundation Council [128]

Prebiotics and Probiotics: What Are They?

A **prebiotic** is defined as 'a selectively fermented ingredient that allows specific changes, both in the composition and/or activity in the gastrointestinal microflora that confers benefits upon host well-being and health' [106]. A prebiotic food is one that escapes digestion and absorption in the small intestine and upon reaching the large intestine, changes the composition or activity of the microbiota selectively, conferring a health benefit [106]. Prebiotics are specialised plant fibres including skin of apples, bananas, onions, garlic, and beans that feed that good bacteria in the large intestine. Many resistant starches act as prebiotics, though not all resistant starches qualify as prebiotics [156]. Prebiotics are needed to feed the good bacteria that make up the gut microbiome.

Probiotics are live bacteria in yoghurt, other fermented dairy products (e.g. kefir) and commercially produced supplements.

See Table 3.10 for some sources of prebiotics and probiotics.

How Do Probiotics Work?

Probiotics are able to boost immunity, eliminate pathogens, moderate effects of antibiotics, aid in digestion and inflammatory bowel disease and can play a role in prevention and treatment of cancer.

Impact on cancer pathogenesis

Lactic acid bacteria are a heterogenous group of microorganisms present in many foods like yoghurt and are often used as probiotics [8, 69]. Some of the actions by which probiotics and the lactic acid bacteria may impact in cancer include prevention of mutations, inhibition of mutagenic activity, decreasing enzymes implicated in the generation of carcinogens, mutagens or tumor-promoting agents, anti-genotoxicity, anti-inflammatory, ridding the body of mutagens, delaying the onset of tumors, suppressing tumors and modulating the immune response including immune cell surveillance [69, 151, 200, 275].

Probiotics and modulation of immune response

Lactic acid bacteria are able to induce modulation of cell-mediated immune responses, activate the reticulo-endothelial system, augment cytokine pathways and regulate interleukins and tumor necrosis factors [151].

Experiments in mice suggest that probiotics such as Bifidobacterium may be able to modulate cancer immunotherapy via facilitation of infiltration of T Cells into tumors, and are able to almost completely halt melanoma growth when combined with a specific antibody therapy [237]. Another study in mice with chemically induced colon tumors found that feeding the mice yoghurt for 6 months resulted in inhibition of tumor growth, and an increased number of IgA-secreting cells and CD4 + T lymphocytes and a decrease in IgG+ and CD8+ cells in the large intestine walls. The researchers concluded that yoghurt may be modulating the immune response by either stimulating the production of cytokines when required or inducing down-regulation of immune cells to avoid an exaggerated immune response [69].

Oral administration of probiotic microorganisms is able to affect mucosal sites outside the colon, as B and T cells can migrate from Peyer's patches to other mucosal membranes around the body (e.g. respiratory, gastrointestinal, genito-urinary tract) as well as to exocrine glands (mammary, prostatic, salivary, lacrimal) [35].

Probiotics and Infection Prevention

Since infections in those who are immunocompromised can add to the burden of cancer patients, and the gut microbiome plays a role in immunity, probiotics may have a role to play in helping prevent infection [213]. It is important that studies of safety and efficacy are conducted [213]. Current advice is for neutropenic cancer patients to avoid probiotic products; however, this advice is based on case reports of bacteraemia and manufacturer's advice and not on solid scientific evidence [213]. It may be found by future research that probiotic supplementation is essential in this cohort of patients.

A systematic review of 17 studies of probiotic use in 1530 cancer patients (756 consuming probiotics, 774 not consuming them) found 105 adverse events in those consuming probiotics and 145 adverse events in those not consuming them. They were unable to establish whether the reported adverse events were associated with probiotic consumption or other causes, and did note that there were five cases of probiotic-related bacteraemia/fungaemia/positive blood cultures [213].

Probiotics and Breast Cancer

In a meta-analysis of 22 prospective cohort studies (1,566,940 participants) and five case–control studies (33,372 participants), intake of yoghurt (and low-fat dairy, but

not other types of dairy) was found to be significantly associated with lower risk breast cancer [287]. A case–control study found that consumption of drinks containing *Lactobacillus casei* Shirota and soy isoflavone was found to be inversely associated with breast cancer in Japanese women who had consumed this regularly since adolescence [250]. The combination of the two seems to be beneficial—rat experiments have shown that soy milk can prevent development of mammary tumors whilst *L. casei* Shirota is able to suppress tumor growth [140].

Studies in breast cancer mice models found that kefir contains several substances that have an immunomodulatory capacity and prevent particular types of cancer [267], as well as retard tumor growth (the mechanisms involved included decreased cytokine IL6 and increased IL10 [68] and increase apoptosis [70]). What was interesting was that the tumor-preventing activity was due to substances released during the fermentation process and not the microorganisms themselves [68]. Other research has shown that lactic acid bacteria supplementation inhibited tumor development in mice through stimulation of the host immune cells, by triggering of CD4+ CD25+ lymphocytes. When these cells were transplanted into other mice, they conferred anti-neoplastic protection in the recipients [154].

Probiotics and Colon Cancer

There is growing evidence of the role of lactic acid bacteria in prevention of colorectal cancer, with a wide range of studies indicating that lactic acid bacteria can interfere with cancer pathogenesis pathways [292]. Lactic acid bacteria have been found to inhibit colorectal cancer initiation or progression through multiple pathways [292]. There are several potential mechanisms by which lactic acid bacteria may play a role in preventing or retarding colon cancer including influencing the metabolic, immunologic and protective functions of the large intestine [275], for example, modulating the intestinal microbiota, inactivating carcinogenic compounds, inducing apoptosis, antioxidant effects and via epigenetic mechanisms [8, 292]. Ingestion of prebiotics also increases the number and activity of lactic acid bacteria in the human colon [275]. Lactic acid bacteria and prebiotics that enhance them are able to deactivate genotoxic carcinogens [275]. In addition, probiotics may be able to provide protection against colon cancer by suppressing the expression of COX-2 [269].

Other Cancers

Lactobacillus species have been found to be associated with promotion of clearance of Human Papilloma Virus-related abnormalities in cervix cells [264] and in animal studies, lactobacillus has been found to inhibit fibrosarcoma tumor growth, activating macrophages and high levels of TNF-α [202], and protect against liver cancer [150], detailed elsewhere [8].

Concomitant Use in Chemotherapy

Probiotics may help alleviate some of the side effects of chemotherapy. Patients undergoing chemotherapy who were administered Bifidobacterium breve strain Yakult had reduced frequency of fever and a lower use of antibiotics than a comparison placebo group. Those in the placebo group also had greater disruption of their intestinal microbiota after chemotherapy including an increase in levels of Enterobacteriaceae compared with the probiotic group [268].

Diarrhoea can also be a side effect of chemotherapy as well as antibiotic therapy, and can contribute to increased hospital admissions in cancer patients [213]. A systematic review found that probiotics may decrease the frequency and severity of diarrhoea in cancer patients, as well as need for anti-diarrhoeal medication, though more studies are needed [213].

Principle 13: Avoid Foods that Interfere with Sleep

Certain foods can interfere with sleep and are best either avoided, or eaten earlier in the day. Many people with cancer have problems with sleep. Sleep is vital for the body and mind's regeneration (see Chap. 4 for more details).

Examples of foods and beverages to avoid if a patient does have problems sleeping include very spicy foods, energy drinks, teas and coffee, alcohol, soft drinks and cheeseburgers. See Chap. 4 (Table 4.3) for more details.

Principle 14: Pay Attention To Food Cooking and Storage Methods

Some food preparation processes such as salting, smoking, charcoal-cooking and broiling are carcinogenic [75]. The World Cancer Research Fund and American Institute of Cancer Research Second Expert Report found that processed meat is a cause of cancers of the oesophagus, lung, stomach and prostate [276].

The report also stated that Cantonese-style salted fish is a probable cause of nasopharyngeal cancer [276].

Cooking Meat

The World Cancer Research Fund and American Institute of Cancer Research Second Expert Report found that there is 'limited evidence' that animal foods that are grilled/broiled, barbecued/charbroiled) or smoked are a cause of stomach cancer [276].

When muscle meat (beef, pork, poultry, fish) are cooked at high temperatures, heterocyclic amines are formed (from amino acids and creatine) and these can pose a cancer risk. The cooking methods that produce the largest amounts are frying, grilling (broiling), and barbecuing (charbroiling) as these use very high temperatures. Meats cooked via oven roasting and baking involve lower temperatures, and therefore produce less heterocyclic amines (though be warned, the gravy from meat drippings contains substantial amounts). Meats that are partially cooked in a microwave oven before being cooked by other higher temperature methods also have lower levels of these chemicals [276].

Polycyclic aromatic hydrocarbons (PAHs) are formed when meat is burnt incompletely. When meat or fish is cooked with intense heat over a direct flame e.g., grilling (broiling) or barbecuing (charbroiling), fat dripping onto the hot fire produces PAHs that can stick to the surface of the food, and the higher the heat, the higher the level of contamination. Using wood creates more PAHs than charcoal [276].

Hint for Cooking Meat
Cooking at lower temperatures is generally a healthier method of cooking meat than cooking at higher temperatures.

Cooking and Acrylamides

As discussed previously under **Principle 10** Avoid Foods Containing Acrylamides, cooking particular foods at high temperatures (>120 °C) can create dangerous acrylamides.

Microwaving

Care should be taken with microwaving food—plastic containers that are not microwave safe and plastic wrap covering foods should be avoided as they can produce toxins. If food is microwaved at higher or prolonged temperatures, or if water is added, this can destroy nutrients. Non-stick pans can also release toxins if the surface is damaged or temperature too high [273].

Cooking and Nutritional Value

In general, the less processed the food is, the more nutrients it retains and the better it is for you. Most forms of cooking reduce the overall nutrient content of

vegetables. Raw foods retain the most nutrients, then in order: steamed, baked, boiled and fried (least retention). Boiling liberates 50% of important nutrients into the water. However, cooking also increases the bioavailability of some nutrients and therefore some foods should be cooked (see next section).

Vegetables should be lightly cooked, for example steaming for 5 min to soften them whilst still retaining the nutrients. Brief scalding in hot water is fine, but prolonged boiling should be avoided. Roasting or grilling or briefly stir frying are also acceptable methods of cooking to retain flavour and nutrients. Stir frying at high temperatures for lengthy periods should be avoided as it destroys many of the nutrients. If frying, it should be done quickly with either water, or with oils with a high smoke point (high heat tolerance) such as sesame oil, rice bran oil or macadamia nut oil.

Some Foods Should Be Cooked

Some foods are better cooked as it increases the bioavailability of key constituents. The bioavailability of carotenes, for example, is increased by cooking and pureeing vegetables, in particular by adding oil since carotenes are fat soluble [276].

Cooking and processing tomatoes increases the concentration and bioavailability of one its key active constituents, lycopene, and when cooked and eaten with oil-rich foods, this greatly increases its absorption from the digestive tract [273, 276]. Lycopene is four times more bioavailable when derived from tomato paste than from fresh tomatoes [276].

Cooking with Oils

The smoke point of oils is the temperature beyond which it begins to smoke and gives off toxic smoke. A high smoke point is desirable if you are going to cook (fry) with oils. The smoke points if several oils are set out in Table 3.11.

Table 3.11 Smoke points of common oils

Oil	Smoke point
Olive oil	210 °C [193]
Sesame oil	210 °C [193]
Grape seed oil	252 °C [193]
Avocado	249 °C [193]
Macadamia nut oil	196 °C [193]
Coconut oil	177 °C [24]
Rice bran oil	254 °C [24]

Some Wisdom from the Orient: Eating from the Chinese Medicine Perspective

Many in the west advocate eating raw vegetables in preference to overcooked vegetables. From a Chinese medicine perspective, however, raw and cold foods can be damaging to the digestive system (termed the Pi and Wei in Chinese, which translates to 'Spleen' and 'Stomach' respectively, the Spleen being an entirely different concept in Chinese medicine than what it is in biomedicine). When a person has cancer, particularly if they have undergone treatment such as chemotherapy, it is likely that their 'Spleen/Stomach' has become weakened. If this was the case (and this would need to be diagnosed by a Chinese medicine practitioner), then raw foods and cold foods (e.g. ice cream, salads, raw juices) should be minimised or avoided and instead warm, cooked foods eaten. Raw juicing would be considered potentially damaging to the 'Spleen/Stomach' if consumed excessively.

The Bigger Picture: Health Information and the Forces at Play

At the systemic level, there are some strong forces at play in the world of food, as there are in medicine—these are the companies that make billions of dollars from people consuming their products and it's not just the obvious fast-food chains. These companies and people who control them have a vested interest in the kinds of information that reach the public, and their marketing is fierce and convincing. As clinicians, we need to be aware that big food organisations play a big part in determining national dietary guidelines and ensuring that these don't damage their business. For many years, the Australian and other national heart foundations in other countries were warning us that butter, cheese and eggs were no good for cardiovascular health. Now, the Australian and other international guidelines deem these not so detrimental to our health. We only have to remember the influence that the cigarette industry had, with medical doctors advertising cigarettes as being soothing for the throat in the middle of last century, despite the fact that German scientists had already identified that smoking was a cause of lung cancer decades previously.

Additionally, in the world of medicine, there is big money in cancer, as there is in other chronic illness. The Pharmaceutical Industry may not be so welcoming to programs and incentives promoting nutrition as a preventative and/or adjunct treatment to cancer. This is substantiated by the very minor role that diet plays in medical degrees, medical journals and, in particular, in medical research. This is a strong indication of the value status given to nutrition and its role in prevention and treatment of disease.

Voicing Concerns About Contamination of Our Food Supply

Unfortunately, what types of foods we are able to procure on a daily basis is not always within our control and the information about it can be confusing and contradictory. We are, for the most part, dependent on others for our food, and more and more, that food supply chain is becoming adulterated or it is nutritionally lacking. Where we live and our socioeconomic situation also impact on what kinds of foods we can buy for ourselves. Organic foods, for example, are more expensive and hard to find in some places. As healthcare practitioners, we have a role to play in voicing our concerns about the impact of environmental toxins on our food supply, as do our patients. Who else will stand up if we don't?

Reductionism in Research

As clinicians, we need to understand how research is conducted and how to interpret it. Our scientific research methods are inherently reductionist in nature. If we apply this reductionism to the study of nutrition, when we try to isolate active constituents in foods instead of looking at whole foods and combinations of foods as diets, we are likely to miss some very important information. Single nutrient studies, though essential for understanding their function, are often not very useful for the clinician with a patient who has nutrient-related problems. Importantly, the importance of the social benefits of eating with others, such as the opportunity to unload stresses, should not be underestimated, though this is rarely considered in dietary studies.

Conclusion

At the end of it all, a healthy patient will do better than an unhealthy one, no matter what the health disorder. Research supports the notion that if you improve your diet, you will live longer. Nutrition is one of the essential pillars of health, along with stress reduction, sunshine (vitamin D), physical activity and sleep. Diet is one modifiable factor in people's lifestyles that can contribute to prevention of cancer, and in a person with cancer, their road to recovery. However, it is difficult for people to change their diets as diets are habits, typically lifetime habits. Thus, changing diet is about practice—practising new habits. Practice makes perfect and it takes discipline, not unlike the discipline of sportswomen and sportsmen who train day in and day out. One trick is for the patient to make one small change every day and reward herself/himself for making that change. The size of the reward

should be greater than the degree of change. A simple, individualised strategy on paper, for example incorporated into a Wellness Plan, works well.

We, as clinicians, are there to give guidance, using the best evidence we have, and to play the role of the coach also, encouraging our patients to make steps, however incremental, toward a better lifestyle that includes a healthy diet. Eating should be pleasurable. There is no point in imposing strict dietary measures on a patient if, in the end, it will just make them miserable. Some common sense needs to prevail. The social context of eating, with friends and family, where stresses can be unloaded, is likely to be almost as important as what one eats, yet it is rarely thought of when diet is considered. Please consider.

Additional Reading Section

- **Omega 3 and Omega 6 (Section: Principle 7 Include Good Sources of Dietary Fats and Oils and Avoid Unhealthy Ones)**
- **Green Tea (Section: Principle 8 Keep Hydrated But Choose Your Drinks Wisely, Sect. 8.3)**.

Section Principle 7: Include Good Sources of Dietary Fats and Oils and Avoid Unhealthy Ones

Omega 3 and Omega 6

More On the Evidence that $n-3$ PUFAs Decrease Risk of Cancer

Population studies indicate that the incidence of prostate cancer is high in North America and northern Europe but low in Asia. In Japan, intake of $n-3$ PUFAs is around eight times that of Americans (and blood levels are twice that of Americans); however, prostate cancer rate was 22.7 per 100,000 in 2008 compared to 83.8 per 100,000 in the US [278]; in 2012, the prostate cancer incidence was 13.6% in Japan compared to 28.3% in the US [279]. Conversely, a 2013 study found that higher blood levels of Omega 3 were associated with increased risk of prostate cancer [36], however, the study has been widely criticised on a number of levels and was methodologically flawed [1]. A more recent review found that cohort studies suggested an association between higher intake of fish and decreased risk of prostate cancer-related death. It concluded that overall, there was insufficient evidence to suggest a relationship between fish-derived $n-3$ PUFAs and prostate cancer risk; however, an association between higher $n-3$ PUFA intake and decreased prostate cancer mortality may be present, and more studies were needed [10].

Not all the evidence is positive, and an earlier systematic review found that Omega-3 intake was not associated with incidence of various cancers with the reviewers concluding that dietary supplementation with $n-3$ PUFAs was unlikely to prevent cancer [169]. A likely reason for this is that simply not enough $n-3$ PUFA's were consumed. Where supplements are involved, the quality of the supplements is very important and may impact results substantially.

Anti-cancer Mechanisms of $n-3$ PUFAs

Omega-3 fatty acids are likely to exert anti-cancer effects by impacting several different pathways associated with cancer pathogenesis including cell proliferation, cell survival (including promoting apoptosis), angiogenesis, inflammation, metastasis and epigenetic abnormalities [136].

Several studies have demonstrated that $n-3$ PUFAs, EPA and DHA, can inhibit tumor growth by inducing cancer cell apoptosis, alone or synergistically when combined with conventional chemotherapy (where they may improve efficacy and/or tolerability) [56, 64]. The cytotoxicity of $n-3$ PUFAs is confined to cancer cells—research indicates little or no toxicity to normal cells—and it has the potential to sensitise tumor cells, potentially improving their efficacy [64]. Both EPA and DHA have anti-inflammatory properties and are able to decrease arachidonic acid-derived eiconsanoids and decrease production of pro-inflammatory cytokines as well as decreasing reactive oxygen species and lymphocyte proliferation [214].

PUFAs have a regulatory ability and can both inhibit or facilitate apoptosis depending on the circumstances. They selectively affect the Toll-Like Receptor family and influence the activity of NFκB downstream. NFκB is a transcription factor that is active in most tumor cells (hematopoietic, prostate, breast cancers), and controls genes involved in apoptosis, inflammation, cell adhesion, proliferation, the adaptive immune response, the stress response, and tissue remodelling. Disruption of NFκB signalling leads to inflammatory diseases and cancer. In tumors, suppression of NF-kB activity inhibits proliferation, causes cell cycle arrest, and leads to apoptosis [60].

Omega-3 oils are also beneficial for brain function and mental health, cardiovascular function, and protection against inflammatory disorders.

Benefits of $n-6$ PUFAs

$n-6$ linoleic acid, found in many plant oils, is metabolised to γ-linolenic acid (GLA) which is converted to dihomo-γ-linolenic acid (DGLA). DGLA is a precursor to prostaglandin PGE1 (involved in inhibition of platelet aggregation and inflammation, produces vasodilation, regulates immune responses and reduces blood pressure and inhibits cholesterol biosynthesis) and 15-OHDGLA which inhibits formation of pro-inflammatory compounds from arachidonic acid (e.g.

PGE2 and 4-series leukotrienes) [96]. DGLA is also converted to arachidonic acid through the action of D-5 desaturase; however, because human D-5 desaturase has limited activity, production of PGE1 and 15-OHDGLA from DGLA is preferred over production of arachidonic acid. Arachidonic acid is then converted to EPA, and EPA is then converted to DHA [96]; however, arachidonic acid can also produce a range of pro-inflammatory compounds [96].

Dietary forms of GLA include evening primrose oil, borage oil and blackcurrant seed oil as well as other foods [96]. Dietary GLA reduces the synthesis of potent inflammatory mediators from arachidonic acid [214] and has been found to be beneficial in a range of health conditions including general inflammation, hypertension, diabetic neuropathy, rheumatoid arthritis and skin conditions [96]. Arachidonic acid does play useful roles, however, including helping make up cell membranes and is used within the body to make substances involved in regulating inflammation, blood clotting and cell communication.

Critical Ratio of *n* − 3: *n* − 6 PUFAs

Despite *n* − 3 and *n* − 6 PUFAs both having a range of beneficial actions in the body, the ratio of *n* − 6: *n* − 3 is important. The major sources of *n* − 6 and *n* − 3 PUFAs, linoleic acid and α-linolenic acid respectively, are desaturated by the same enzyme human D-6 desaturase, leading to competition between the two fatty acid groups [214]; this enzyme is often impaired in the western diet and generally favours the *n* − 3 pathway [96].

High levels of *n* − 6 PUFAs or a high *n* − 6: *n* − 3 PUFA ratio promotes inflammatory conditions and diseases such as cancer and cardiovascular disease, whereas increased levels of *n* − 3 PUFAs or a low *n* − 6: *n* − 3 PUFA ratio is suppressive for such conditions [235].

Western diets are excessive in the amount of *n* − 6 and deficient in *n* − 3 PUFAs with the ratio of *n* − 6 to *n* − 3 PUFAs 3 in western diets somewhere between 10:1 or 25:1 [235, 236, 273]. In contrast, it is likely that humans evolved on a diet where this ratio was 1:1 [235]. In patients with colorectal cancer, a diet characterised by a ratio of 2.5:1 (*n* − 6: *n* − 3 PUFAs) reduced rectal cell proliferation; however, a ratio of 4:1 had no effect in reducing rectal cell proliferation. The optimal ratio is likely to differ from disease to disease [235].

Section Principle 8 Keep Hydrated But Choose Your Drinks Wisely Section "Tea"

Tea and Cancer

There have been only a few randomised controlled trials, two of which examined the effects of tea on urine levels of 8-hydroxydeoxyguanosine (8-OHdG), a

biomarker of oxidative DNA damage that may be a predictor of increased cancer risk. In one, 133 adult heavy smokers were randomly assigned to drink four cups of either decaffeinated green tea, decaffeinated black tea, or water daily for 4 months. Green tea drinkers had a significant (31%) decrease in urinary levels of 8-OHdG whilst there was no change in black tea drinkers, indicating that green tea may protect smokers from oxidative damage and reduce cancer risk caused by smoking-associated free radicals [111].

In another study, 124 individuals at increased risk of liver cancer due to hepatitis B virus infection and aflatoxin exposure were randomised to receive either 500 mg (equivalent to two cups of tea) or 1000 mg of a green tea polyphenol supplement or a placebo daily, for 3 months. Both green tea supplement groups had substantially lower urinary 8-OHdG levels at the study, suggesting that green tea polyphenols are effective in reducing oxidative DNA damage [168].

Cell culture research demonstrated that black and green tea extracts have anti-mutagenic, anti-proliferative and anti-neoplastic activity. Both black and green tea extracts were able to inhibit neoplastic transformation in mouse mammary organ cultures, rat tracheal epithelial cells and human lung tumor epithelial cells, and were able to strongly inhibit benzo[a]pyrene adduct formation with human DNA, as well as enhance induction of phase II enzymes, glutathione-S-transferase and quinone reductase and inhibit free radicals [240]. Studies in humans have found external application of green tea extract protects against UV(B) damage [83].

Green tea may be beneficial in other conditions including hypercholesterolemia, artherosclerosis, Parkinson's disease, Alzheimer's disease, and other ageing-related disorders [288].

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