Nestlé
Good Food, Good Life

Food and Nutrition Communication

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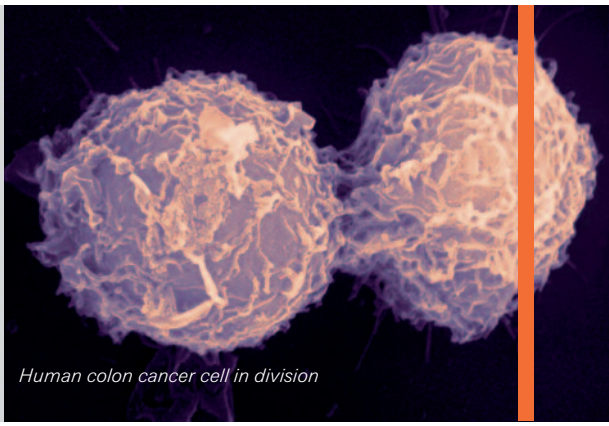
Nutrition and Cancer

Cancer is a subject that strikes terror into the hearts of those diagnosed with the disease. Fifty years ago, euphemisms such as the "cruel disease" were used in order to avoid even mentioning the word "cancer". Times are changing, however, and to judge by the bookstore success of works such as those of David Servan-Shreiber to name but one author, many people have braved the taboo, and are becoming increasingly interested in ways of improving their chances of avoiding the many types of cancer. Reinforcing the immune system, managing stress and anxiety, living in an unpolluted environment and eating the right type of food can diminish the risk.

In this edition, we provide some basic background to the subject and try to answer a few questions about risk, especially as regards what we eat and drink.

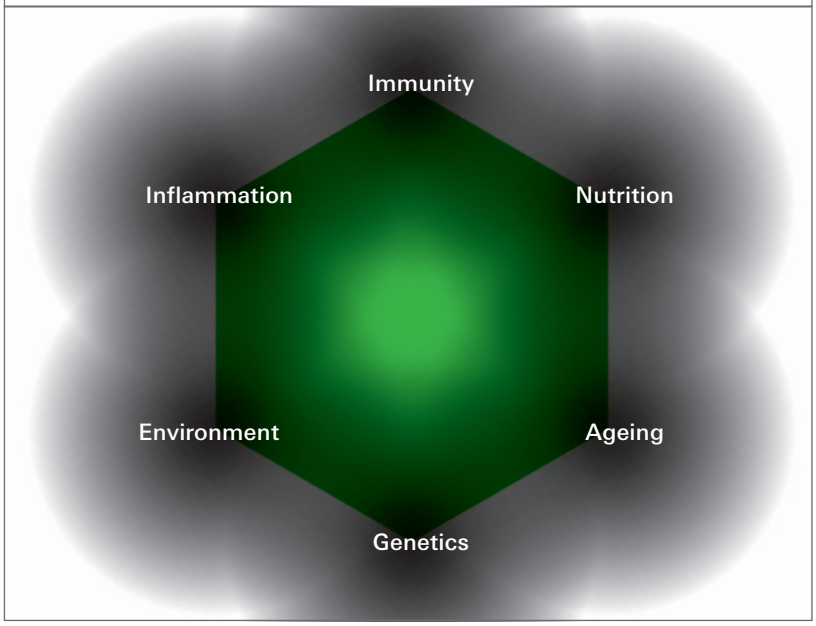


Human colon cancer cell in division

Although the field of nutrition and cancer is extraordinarily complex, some new knowledge is encouraging. The 4th Nestlé International Symposium recently hosted Nobel Prize-winning participants to discuss nutrition and cancer, from cell biology to patient management. As Professor Günter Blobel, Nobel Prize laureate in Physiology for Medicine 1999 and Nestlé Nutrition Council member pointed out in his opening remarks, the best means for further reducing cancer are prevention and early detection. This is where a healthy diet and lifestyle can put the best chances on our side.

At the same time, special nutrition is being developed for cancer patients, and has made remarkable progress in recent years.

Multiple Factors Influence Cancer Development



The Development of Cancer

"No man, even under torture, can say exactly what a tumour is"
J. Ewing 1916

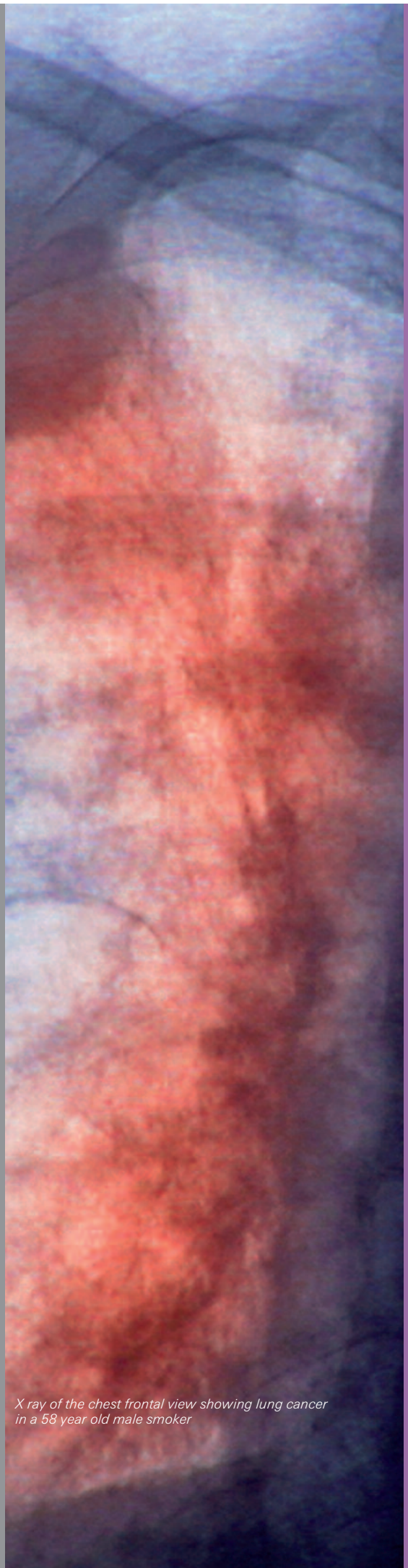
Perhaps Ewing can now be proved wrong!

Most of us are aware that cancer develops as body cells proliferate abnormally and build up into tumours, indicating a disruption of the body's highly complex equilibrium, and a failure of the immune system. While normal cells can only divide a finite number of times before ending the cycle of cell division and dying, cancer cells have the ability to divide endlessly without displaying the normal "ageing" seen in non-cancerous cells. In many cancers this is due to the activation of an enzyme, telomerase, that maintains the integrity of the chromosomes during cell division. Cancer develops in stages. The first stage of the disease, called "initiation", occurs when a normal cell is exposed to a carcinogen, such as a chemical, a virus, radiation, or even specific dietary factors. Essentially, anything that causes damage to the cell membrane or the DNA material (our individual genetic code) within the cell can be classified as a carcinogen or a mutagen. Fortunately, DNA repair mechanisms can usually restore the cell to its normal state. If the cell is unable to repair itself, however, it changes or "initiates". An initiated cell passes on this change when it replicates, thus advancing from the initiation to the "promotion" stage. At the promotion stage, the cell may experience spontaneous remission back to the initiation stage, or it may be exposed to growth inhibitors or "antipromoters", such as antioxidants and phytochemicals, that will allow regression back to the initiation stage.

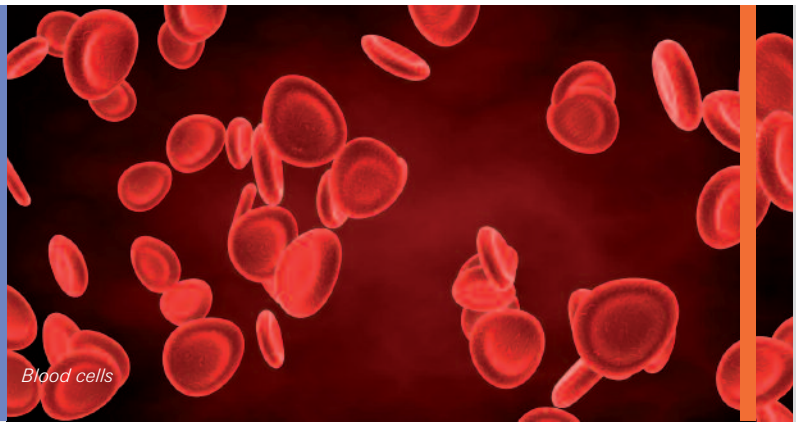
However, the damaged cell may eventually lose its DNA integrity and develop into a pre-malignant lesion such as dysplasia, carcinoma *in situ*, or polyps. As the cell continues to lose control over its function and structural integrity, progression to the clinical stage of cancer occurs, with disruption

of normal body functions. The entire process, from exposure to a carcinogen to development of cancer, often takes years.

*NB: **The Nestlé Research Centre** reminds us that a distinction should be made between a mutagen and a carcinogen. A mutagen causes DNA modifications that may or may not lead to cancer. A carcinogen is a substance that has been shown experimentally to cause cancer. This can be either by causing mutations in the DNA or by its "promoting" effects such as the stimulation of cell growth, inhibition of cell death, etc. A mutagen can only cause a DNA modification by interacting with the DNA. A cell that is "hit" by a mutagen/carcinogen, acquires some properties that predispose it for growth. The initiated cell can also be eliminated by apoptosis (programmed cell death). Cell proliferation is an obligatory step to "fix" a mutation, i.e. to adapt the second DNA strand to represent a copy of the mutated base in the first strand. Otherwise DNA mutations are very rapidly detected and repaired by DNA repair enzymes. Even after a mutation has been "fixed" it is not certain that a tumour will form. Only a few lesions progress to cancers. In general, a second "hit" (mutation of other event) is necessary for the cell to become "transformed", and grow independently. It will have lost its natural contact inhibition, i.e. the capacity to respond to neighbouring cells to suppress their growth. These cells often grow without the need of growth factors and many oncoproteins (derived from genes that are mutated in cancer cells) are growth factors or signalling molecules and provide for growth-factor independent growth. Loss of DNA integrity is a late stage in the genesis of tumours.*



X ray of the chest frontal view showing lung cancer in a 58 year old male smoker



Blood cells

Tumours require a blood supply – Angiogenesis

Normal cells do not divide unless they receive external signals that cause the cells to enter the cell division cycle. Cancer cells, however, can divide even in the absence of these external factors and are therefore immune to many of the normal regulations of cell division. The cancer cells no longer function as a part of a larger organism, but behave more like independent entities living without regard for the organism as a whole. A single cell dividing without proper growth-signals results in a population of rapidly dividing, growth factor-independent cells. The resulting mass of cancer cells, or tumour, soon becomes large enough to need a new blood supply in order to provide oxygen and nutrients, and remove waste products. Without a blood supply, the cells in the middle of the tumour will die off. In fact, tumours without a blood supply are unable to grow more that about one millimetre across. As soon as they start growing, tumours release small, hormone-like molecules that cause nearby blood vessels to start growing towards the tumour until they actually form a new branch supplying the tumour with blood. Drugs have now been developed that, in laboratory animals, can prevent new blood vessels from developing. Some of these drugs are already in trial in human beings with cancer. They show considerable promise in this new therapeutic approach to deprive the tumour of a blood supply.

Free Radicals and the Role of Inflammation

Oxidation is the chemical process that causes metal to go rusty and sliced apples to turn brown. The same process occurs in the body and can harm cells. Free radical molecules are responsible for this oxidative damage. Free radicals can be contained in (or induced to form) by a variety of things including tobacco smoke, radiation (e.g. sunlight or x-rays) and even the normal functioning of the human body. In fact our life in an oxygen-containing environment is only possible via redox reactions and of radical intermediation.

Atoms are composed of a nucleus, containing protons and neutrons, and a group of particles (electrons) that constantly circle the nucleus.
In most molecules, electrons travel in pairs around the nucleus. Free radicals are an exception.
At least one atom in a free radical has a single (unpaired) electron circling the nucleus. This single electron gives the atom a charge, making it powerfully attracted to other molecules. A molecule with an unpaired electron is said to be "radicalized". These radicalized compounds, or "free radicals", quickly react with surrounding molecules. For this reason these compounds are also called reactive species. Oxygen is the most common reactive species found in the human body and when it acquires an extra electron it is called a reactive oxygen species (ROS).

To sum up: free radical species attract an electron from a nearby molecule so that all of its electrons are in pairs. The affected target molecule will then become a radical. A chain-reaction of electron attraction or 'theft' can occur within a cell. Free radicals can affect just about any structure in a cell this way, including DNA. If free radicals steal an electron from DNA, there can be damage to the genetic code and interference with cell function. DNA damage due to free radicals has been associated with ageing, rheumatoid arthritis, inflammatory bowel disease, acute respiratory distress syndrome (ARDS), emphysema, and some cancer types.

An accumulation of oxidatively damaged proteins may occur in the tissues when proteolysis and the orderly cell cycle transitions are perturbed. Oncoproteins may then begin to build up.

Infection and inflammation are primary causes for increased ROS formation in living organisms. The diet can also provide and increased burden, e.g. a high fat diet, loaded with oxidized fats and oxidized free fatty acids can promote free radical generation/propagation after ingestion.

Antioxidants

Antioxidants can stop free radicals before they cause damage. Compounds with antioxidant properties do this by donating an electron to a free radical, often without needing to steal another electron. Unlike most compounds, antioxidants are stable with or without the electron they donate. Some antioxidants home in on and neutralize free radicals by forming permanent bonds with them.

If we adopt a healthy lifestyle, we need not overestimate the dangers of free radicals, nor become unduly alarmed. Our life in an oxygen-containing environment is possible because of the unique chemical properties of oxygen, (which itself contains two unpaired electrons). Free radicals are thus essential by-products of our aerobic metabolism. Evolution has provided efficient systems to keep free radicals in check. Only with inadequate nutrition, or in response to disease and other stress factors do these endogenous antioxidant systems become overwhelmed.

Food Sources of Antioxidants

There are many good sources of antioxidants including green tea, berries, tomatoes and soy. Examples of dietary antioxidants include vitamins C and E. Antioxidants can be found in many fruits and vegetables because plants produce antioxidants to help protect themselves from free radicals generated by solar rays.

The body naturally produces antioxidants that help protect against free radical damage, but human beings also obtain antioxidants from food sources.

As we have mentioned in previous editions of *Food and Nutrition Communication*, just because something is healthy does not mean "the more the better". Even healthy substances such as vitamins can cause harm if taken in excessive amounts. This is not usually the case with food intake, but it can be with pharmaceutical supplementation. *(See Food and Nutrition Communication Vitamin Intakes – How much is too much and how much is not enough?)*.

Nutrition and the Reduction of Cancer Risk

Over the past two decades, it has become increasingly clear that what we eat plays a significant role in the risk of cancer. It is estimated that approximately 30 to 40% of all cancers are linked to diet and related lifestyle factors. At the population level, simple changes in eating patterns could therefore have a dramatic impact on reducing cancer rates.

Some food components, for example the isoflavones of soya beans act in a similar way to hormones, which may help to protect against hormone-dependent cancers such as endometrial and ovarian cancers, especially in post-menopausal women. More recently, it has been discovered that food compounds (such as sulforaphane in broccoli) can encourage the body's production of protective enzymes, called ***phase II enzymes***. These enzymes help to detoxify cancer-causing substances and prevent cell damage that can lead to cancer. Other such foods include cruciferous vegetables (e.g., cabbage, cauliflower, brussels sprouts, and bok choy), garlic, onions, berries, and grapes.

Certain components in "functional foods" may also be able to help to delay, or inhibit the advancement of cells to the clinical stage of cancer. However not everyone derives benefit from functional foods. An individual's genetic makeup most likely influences

The Nestlé Research Centre *comments that the antioxidants that can trap ROS need to be at sufficiently high concentrations close to the site of ROS generation. Otherwise the ROS will react with the first molecule it encounters on its way, primarily proteins and lipids but also DNA. Endogenous antioxidant systems seem to have a much more powerful effect than those ingested with food. The latter do stimulate phase II enzymes but there is no "complete protection" either from endogenous or exogenous sources.*

the extent of the response to functional food components. This may explain why some people seem to experience positive effects from functional components of food, while others do not.

Whole Foods and Prepared Foods

Whole foods, such as fruits and vegetables, represent the simplest examples of functional foods. Prepared foods, such as breads, cereals, dairy products, and juices, which have been enriched or fortified with natural or scientifically developed nutrients, are also functional foods. Some of the newer examples may include foods enhanced with phytochemicals or "botanicals" (natural plant extracts).

Although it may be possible to isolate specific components of food that may reduce the risk of diseases like cancer, it is unclear whether isolated active compounds added to food have the same health benefits as whole foods because compounds in foods may act synergistically to impart health benefits.

NB: In legislative or regulatory matters, "functional foods" may have a different meaning, ususally a food fortified in some specific ingredient. This would be the subject of a separate publication.

Foods that May Reduce Risk of Cancer

Food	Functional Components[1]	Possible Role(s) in Cancer Risk Reduction
Broccoli and broccoli sprouts	Sulphoraphane	Stimulates the body to produce its own protective phase II enzyme[2], neutralizes free radicals
Tomatoes and tomato products	Lycopene	Potent antioxidant that may reduce risk of prostate cancer, may also stimulate phase II enzymes[2]
Garlic and onions	Allyl sulfides	Boosts levels of naturally occurring enzymes that may help maintain healthy immune system (phase II enzymes[2])
Soyabeans	Isoflavones (genistein and daidzein)	May act as an anti-oestrogen, plugging up receptors for oestrogen which may reduce the risk of oestrogen-dependent cancers; may inhibit the formation of blood vessels that assist tumor growth
Grapes, strawberries, and raspberries	Resveratrol, Ellagic acid, Quercetin	May block the body's production of enzymes needed for cancer cells to replicate, stimulate phase II enzymes[2]
Oranges and lemons	Limonene	Boosts levels of naturally occurring enzymes that may break down carcinogens, stimulate phase II enzymes
Green tea	Polyphenols (catechins)	May help block damage to DNA by neutralizing free radicals and reducing cancer risk, stimulates phase II enzymes[2]
Coffee	Chlorogenic acid	Stimulates phase II enzymes[2]
Red wine	Resveratrol	Phase II enzymes may block some pathways implicated in ageing and cancer
Dairy products	Sphingomyelin Calcium	May inhibit tumor cell growth and induce cell death
Flaxseed	Lignans	Acting as a phyto-oestrogen, may offer reduced risk of certain kinds of cancer
Whole wheat	Phytic acid	May suppress the oxidative reactions in the colon that produce damaging free radicals

1 *These represent just one example of functional components in the corresponding food. Most functional foods contain many active components with potential health benefits.*

2 *Phase II enzymes may block some pathways implicated in ageing and cancer. Other Phase II enzyme inducers not mentioned in the table include curcumin, rosemary extract and chlorophyllin.*

Carbohydrates and Obesity – link to Oesophageal cancer

We tend to think of obesity as linked to cancers of the lower digestive tract. However, recent research has also suggested a link to oesophageal cancer. Oesophageal cancer is the eighth-leading cause of cancer related death in men in the US. Despite recent advances in treatment, the five-year rate of survival for this cancer remains below 20%. While the causes of oesophageal cancer remain largely unknown, US researchers suggest a possible link to dietary intake of refined carbohydrates and obesity. An epidemiological study, published in the *American Journal of Gastroenterology*, says a sharp rise in recent decades of oesophageal cancer — from 300,000 cases in 1973 to 2.1 million in 2001 at age-adjusted rates — parallels the sharp rise in refined carbohydrate intake and obesity during the same period of time.

The study found carbohydrates were unique in that no other studied *nutrients* were found to correlate with oesophageal cancer rates (see also Alcohol, below). Moreover, a high intake of refined carbohydrates has been found to contribute to obesity, which in turn has been named as a risk factor for many types of cancer.

The hope expressed by the team of Dr. Li of Case Western Reserve University/University Hospitals Health System in Cleveland Ohio, is that if the trends in refined carbohydrate intake and obesity can be reduced, the incidence of oesophageal cancer can also be reduced, in parallel.

It must be remembered that this research only shows an association between refined carbohydrate intake and oesophageal cancer; this does not necessarily mean that high intake of refined carbohydrates ***causes*** cancer; this can only be established by further research.

Carotenoids and Prostate Cancer

Lycopene may show benefits against benign prostate hyperplasia (BPH), a condition said to affect more than half of all men over the age of 50.

Pomegranates and Cranberries

Pomegranates, a rich source of antioxidants, have been linked to improved heart health. But a growing body of science indicates that the fruit also improves sperm count, protects against prostate cancer and slows cartilage loss in arthritis. Cranberries, containing proanthocyanidins, have recently been found to help prevent Barrett's oesophagus and other conditions leading to cancer of the throat.

Benign prostatic hyperplasia (BPH) is a non-cancerous swelling in the prostate gland of older men. It affects approximately 25 per cent of American Caucasians over the age of 50. According to the European Association of Urology, 30% of men older that 65 are affected by BPH. According to the European School of Oncology, over half a million new cases of prostate cancer are diagnosed every year world wide, and the cancer is the direct cause of over 200,000 deaths. The incidence of the disease is increasing alarmingly with a rise of 1.7 per cent over 15 years. Forty people took part in the new pilot study from Germany, which adds clinical data to an area previously lacking. According to the researchers in the Jan. 2008 *Journal of Nutrition*, epidemiological evidence has suggested that lycopene-rich tomato based foods can protect men from prostate cancer. One study found that men eating four to five tomato based-dishes per week were 25 per cent less likely to develop prostate cancer compared to men eating tomatoes only rarely.

Curry powder as an anti-cancer ingredient

Researchers from Tohoku University in Sendai, Japan, synthesized and tested 90 variations of curcumin, the yellowish component of turmeric that gives curry its flavour, in a bid to boost its anti-cancer effect. Curcumin has already been linked to having a positive effect on cancer as well as potential benefits for reducing cholesterol levels and improving cardiovascular health.

An anterior view of the right breast Illustration dipicting cancer in glandular tissue and lymph nodes of the breast

Soya and Breast Cancer

A flavonoid and lignan-rich diet may reduce the risk of developing breast cancer in post-menopausal women by about 35%, according to a study at the University of North Carolina, which focused on the dietary intakes of flavonoids, lignans and isoflavones by 1,434 women with breast cancer and 1,440 health controls in Long Island, New York. Results support previous findings from Greece and Italy. While significant risk reductions were observed for high intakes of flavonols, flavones, flavan-3-ols and lignans amongst ***post-menopausal*** women, no beneficial affect was observed for isoflavones, nor for any of the above phytochemicals, amongst ***pre-menopausal*** women. Interest in flavonoids is growing rapidly and a mounting body of evidence, including epidemiological, laboratory-based and randomised clinical trials, continues to report the cancer-fighting potential of a number of different flavonoids, such as isoflavones, anthocyanidins and flavonols. Soya however presents some intolerance problems of its own, which is why it can be said that the jury is still out on its true benefits. Most agree that there is no harm in consuming soya as a food, for example in the form of one glass of soya milk or a soya "yoghourt" each day, but do not generally advise taking soy isoflavones in supplement form.

Fibre-rich foods

Whole grains, a rich source of phytochemicals, bran, fibre, minerals and vitamins, have been gaining increasing attention from researchers, with studies reporting reduced risks of metabolic syndrome, diabetes, and colorectal cancer. One meta-analysis showed a 10-40% risk reduction with the highest intake of whole grain foods. *(See also: Food and Nutrition Communication Oct 2006 The Whole Grain – references 4 and 5)*. Another meta-analysis of 40 studies showed a 2-43% lower risk for gastro-intestinal cancers.

Regarding hormone dependent cancers, several large studies also indicate that dietary fibre affords protection against cancer of the ***uterus***.

For every five grams of dietary fibre per 1000 calories, women may reduce their risk of endometrial cancer by over 20%. Endometrial cancer is the fifth most common cancer among women worldwide – around 7,000 American women die from the disease annually – although incidence of the cancer varies more than 10-fold worldwide. Bringing together the results of one case-cohort study and nine case-control studies, researchers from The Cancer Institute of New Jersey, Robert Wood Johnson Medical School, report a strong protective effect from higher fibre consumption.

Good News about Coffee

Evidence for protective effects of coffee against specific forms of cancer (e.g. in the colon and liver) is available from human epidemiological studies as well as mechanistic studies in laboratory animals and *in vitro* cell cultures. A number of different components present in coffee such as caffeine, antioxidants (chlorogenic acids, melanoidins) and the diterpenes cafestol and kahweol have been implicated as potentially responsible for these effects. They are likely to act via different mechanisms and at different stages of the cancer process. There are also numerous case-control studies indicating a negative correlation between coffee consumption and the incidence of colon cancer. In addition, several studies including at least two prospective trials observed significant inverse association between coffee consumption and the risk of developing cancer of the liver cells.

Two encouraging new findings published in *Gastroenterology*, May 2007, and *Hepatology*, August 2007, suggest that drinking two cups of coffee per day may thus reduce the risk of liver cancer by 30% and four cups per day by 55%.

A word of caution: Although these epidemiological studies indicate an association between coffee drinking and reduced cancer risk, they do not provide conclusive evidence of a cause-and-effect relationship.

Bad News about Alcohol

In the Oxford Textbook of Medicine, it is estimated that 6% of all cancer deaths in the UK are caused by excessive alcohol consumption.

Oral and oesophageal cancers

One review of many studies found that people who drink 6 units a day have triple the risk of oral cancer and double the risk of oesophageal cancer, compared to non-drinkers. That is the equivalent of two pints of premium lager or three standard glasses of wine. The International Agency for Cancer Research says that heavy drinking increases the risks of these cancers by 5 to 10 times. But even light drinking (just three units a day) can increase the risk of mouth cancer.

Alcohol increases the risk of liver cancer

Alcohol is one of the well-known main risk factors for liver cancer. Heavy drinking can lead to cirrhosis, a condition where the liver is repeatedly damaged and scar tissue builds up. Cirrhosis increases the risk of liver cancer.

The risks of liver cancer are even greater if a person is infected with the hepatitis B or C viruses. One in five people with these viruses develop cirrhosis and liver cancer. People with these infections should avoid alcohol, as even small amounts could damage their livers.

Alcohol increases the risk of breast cancer

Even small amounts of alcohol can increase the risk of breast cancer. Several studies have found that every alcohol unit drunk on a daily basis increases the risk of breast cancer risk by about 7–11% in certain circumstances. A study funded by Cancer Research UK estimated that alcohol causes about 2,000 breast cancer cases every year in the UK. There is unlikely to be a safe level of alcohol intake.

Alcohol increases the risk of bowel cancer

Studies have recently shown that alcohol can increase the risk of bowel cancer and even small amounts can have an effect. The EPIC study found that for every 2 units a person drinks each day (less than a pint of premium lager) their risk of bowel cancer goes up by 8%. Smoking and drinking together increases risk even more. One study found that the risk of liver cancer was ten times greater in people who smoked tobacco and drank alcohol. A Spanish team found that people who smoke and drink heavily could increase their risk of oesophageal cancer by up to ***100*** times. This problem is made even worse because heavy drinkers and smokers often have unhealthy diets and lifestyles in general.

How does Alcohol cause cancer?

Scientists are not entirely sure how alcohol causes cancer but there are several theories. The strongest one is that in the body, alcohol is converted into acetaldehyde. Acetaldehyde is the chemical that causes hangovers, but it can also cause cancer by damaging DNA and preventing it from being repaired. People who smoke and drink heavily have very high levels of acetaldehyde in their saliva. Other theories include the following:

- Alcohol can increase the level of hormones such as oestrogen in the body. Unusually high levels of oestrogen could cause breast cancer.
- Alcohol makes it easier for dangerous chemicals to be absorbed in the mouth or throat. This includes the many different chemicals in tobacco smoke.
- Alcohol reduces the amount of folate in the blood. Folate is a B vitamin that our cells need to create new DNA correctly. It prevents changes to our DNA that could lead to cancer.
- Alcohol is metabolised by enzymes that can generate ROS.

Red wine does not protect against prostate cancer

One small but widely reported study found that men who drank 4–7 glasses of red wine per week halved their risk of prostate cancer. Red wine contains a chemical called resveratrol, which may have some anti-cancer effects. By decreasing inflammation and ROS, red wine in small doses may help to protect against some cancers and cardiovascular risk. However, two large studies have since found that red wine does not affect a man's risk of prostate cancer. So far, studies have shown that all types of alcohol, including beer, wine and spirits, can increase the risk of prostate cancer.

Alcohol during pregnancy may increase risk of leukaemia in the child

An American study found that women who drank alcohol during pregnancy increased the risk of leukaemia in the child. Two larger studies are now under way to confirm this result. Until their results are available, pregnant women are advised not to drink any alcohol.

The more alcohol consumed the greater the risk, but even very small amounts of alcohol, as little as one drink a day, can increase cancer risk. A team of Italian scientists analysed over 200 studies on alcohol and cancer. They were unable to find any lower daily limit of drinking alcohol where cancer risk was not increased. Because of this, many bodies including the World Health Organisation and the European Code Against Cancer have suggested that women should drink fewer than two units a day, and men should drink fewer than three. While these levels may increase the risk of cancer, the actual effects are likely to be small.

For heavy drinkers, the good news is that it is not too late to start cutting down. UK researchers recently showed that oesophageal cancer risk drops dramatically in heavy drinkers who give it up.

(However, as we have reported several times before, small amounts of alcohol may reduce the risk of heart disease. Heart disease takes an even greater death toll than cancer, so for many, it is a question of balancing the behavioural risks.)

Two non-nutritional cancer risks: Tobacco smoking and Stress

Everyone is aware of the danger of lung cancer associated with smoking. Many people also know about the risk of throat and mouth cancers from smoking. What is less well known among the general public is the association between smoking and pancreatic cancer.

Smoking is the only established risk factor for pancreatic cancer.

The US National Cancer Institute reports that almost 38,000 new cases of pancreatic cancer are diagnosed every year in the US, with almost 34,000 deaths from the disease. British charity Cancer Research UK shows that pancreatic cancer has a poor prognosis overall since most cases are diagnosed quite late. Indeed, only one in every 50 cases will still be living five years after diagnosis.

A new study, part of the Multiethnic Cohort Study of 183,518 residents of California and Hawaii, reports that subjects with the highest consumption of flavonols from the diet had significant risk reductions, compared to the lowest consumption, with ***smokers*** particularly benefiting from flavonol-rich diets because they are already the population most at risk.

The researchers also stated that theirs is the first study to examine prospectively specific classes of flavonols (quercetin, found in onions and apples; kaempferol, found in spinach and some cabbages; and myricetin, found mostly in red onions and berries) and pancreatic cancer risk. Of the three individual flavonols, kaempferol was associated

with the largest risk reduction (22%) across all participants. The interaction with smoking was statistically significant for total flavonols, quercetin and kaempferol.

Another study presented by the German Institute of Human Nutrition Potsdam-Rehbruecke, showed that a diet rich in flavonols from foods such as onions, apples and berries may cut the risk of pancreatic cancer by about 25%. These benefits may be even more pronounced amongst smokers, with a risk reduction of over 59% according to their research.

Stress

Among the factors which dramatically increase the production of inflammatory substances is stress. Clinical observation from as far back as the 18th Century noted that cancer was often preceded by states of severe mental distress and depression.

In the modern world, acute and chronic psychological stress, for example as that created in the workplace, may have profound effects on reactivation of latent or occult cancers among affected persons, through the weakening of their immune systems. In conditions such as burn-out and depression, repeated secretion of noradrenalin and cortisol, hormones that prepare the body for "fight or flight", also prepare the body for inflammation, as a potential wound-healing "emergency" state. For some authors, the in flammatory substances which accumulate almost continuously, may also promote tumours, whether latent or declared.

Recommendations for Cancer Prevention: Results of a Five Year Examination by a panel of the

The World Cancer Research Fund and the American Institute for Cancer Research recently published their seminal report: Food, Nutrition, Physical Activity and the Prevention of Cancer: a Global Perspective.

The report's authors have compiled and processed an unprecedented amount of information on cancer over the last five years, out of which the Expert Panel has set out eight main, general recommendations for the prevention of cancer, with two supplementary recommendations for breastfeeding mothers and cancer survivors.

Briefly, the Eight Recommendations are the following:

1 Body Fat – be as lean as possible within the normal range of body weight.

The median adult body mass index should be between 21 and 23 depending on the normal range for different populations. Keeping slim may be one of the most important ways to protect against cancer and a number of other chronic diseases.

2 Physical Activity – Be physically active as part of everyday life

Be moderately active, equivalent to 30 minutes of brisk walking every day; as fitness improves, aim for 60 minutes. Limit television viewing. Most populations in urbanised settings have habitual levels of activity below levels to which human beings are adapted.

3 Foods and Drinks that promote weight gain

Limit consumption of energy-dense foods, avoid sugary drinks and consume fast foods sparingly, if at all.

e world's leading scientists

4 Plant Foods – East mostly foods of plant origin

Eat at least 5 portions of a variety of non-starchy vegetables and fruits every day. Eat relatively unprocessed cereals and/or pulses with every meal. Limit refined starchy foods. An integrated approach to the evidence shows that mainly plant based, nutrient-dense diets high in fibre protect best against various types of cancer.

5 Animal Foods – Limit intake of red meat and processed meat

Consume less than 500g of red meat per week, and very little if any processed meat. An integrated approach to the evidence shows that animal foods are nourishing and healthy if consumed in modest amounts.

6 Alcoholic Drinks – Limit alcoholic drinks

Limit consumption to no more than two drinks a day for men and one for women. The evidence on cancer justifies a recommendation not to drink alcoholic beverages. Other evidence shows that modest amounts of alcoholic drinks are likely to reduce the risk of coronary heart disease.

7 Preservation, Processing, Preparation – limit consumption of salt. Avoid mouldy cereals, grains or pulses.

Avoid salt-preserved, salted, or salty foods. Ensure an intake of less than 6g of salt per day. Do not eat mouldy cereals, or pulses. Salt and salt-preserved foods are probably a cause of stomach cancer, and foods contaminated with aflatoxins are a cause of liver cancer.

8 Dietary Supplements – Aim to meet nutritional needs through diet alone.

Dietary supplements are not recommended for cancer prevention. High dose nutrient supplements can be protective against some cancers but can be a cause of others. A general recommendation to consume supplements for prevention might have unexpected adverse effects.

The two supplementary recommendations:

1 Breastfeeding

The authors of the report endorse WHO policy on exclusive breastfeeding for babies up to 6 months of age, as epidemiological evidence from prospective and case-controlled studies indicate that lactation corresponds to a decreased risk of breast cancer and a limited risk reduction in ovarian cancers in mothers.

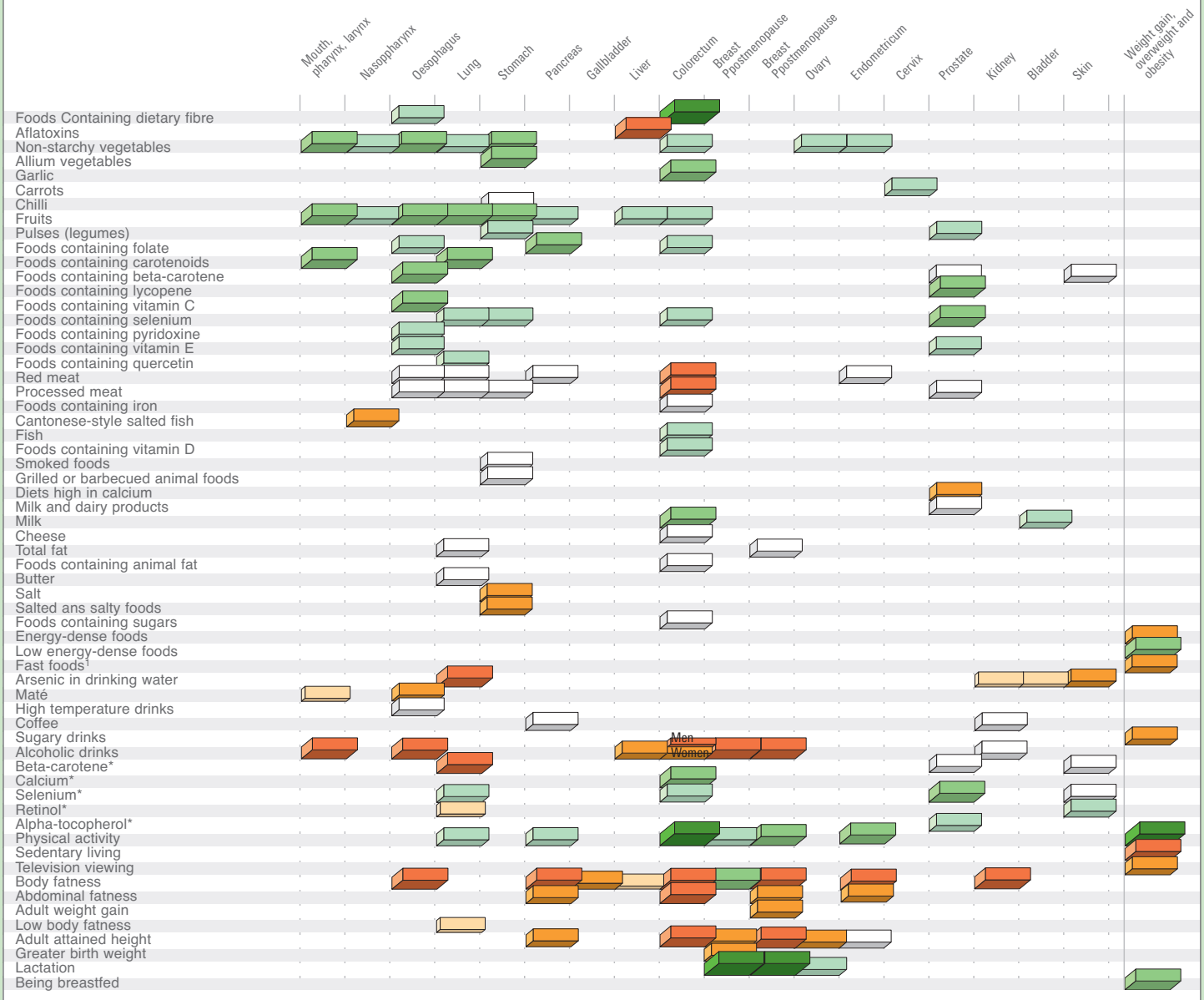
2 Cancer survivors

Follow the recommendation for cancer prevention. All cancer survivors should receive nutritional care from an appropriately trained professional and if able, should follow the recommendations above. There may be specific situations where this is not possible, for example when the gastrointestinal function has been compromised.

The Nestlé Company is aligned with the Recommendations both of this Panel and those of the WHO/FAO Expert Consultation N° 916.

The Panel's judgements

The judgement of the Panel on Food Nutrition, Physical Activity and the Prevention of Cancer: the table summarizes the strength of evidence of the causal relationship of certain foods, types of activity and weight gain with different cancers.



*The evidence is derived from studies using supplements
†Judgement for physical activity applies to colon and not rectum

Re-drawn from the WCRF/AICR Report

Woman undergoing radiation therapy.

Nutrition at Nestlé

The Corporate Wellness Unit and its global network has the role of driving the nutrition, health and wellness initative throughout the company. This means having every company employee trained in nutrition through the NQ programme at basic, advanced or specialized level. It means having all our products put to the test with an evaluation tool known as 60/40+, which rates consumer taste preferences and the nutritional value of our products compared to those of our competitors. It means innovating and renovating the product range, notably through the reduction of sugars, salt, saturated fat and trans fatty acids, providing nutrition information on all the product labels in the form of the "nutritional compass" in order to help consumers make informed choices, reviewing product recipes to make sure they have a solid nutrition foundation, reviewing portion sizing to help people manage their weight, and helping to develop new products for all ages based on exciting new developments in nutritional science and technology.

Nutrition in Cancer Treatment

In order to destroy cancer cells, strong treatments are required during which a certain number of healthy cells may also be damaged. It is this damage to healthy cells that produces the unpleasant side effects which cause eating difficulties. These vary in severity from patient to patient and are now better controlled by newer drugs.

Nausea or lack of appetite are the most frequent problems. It is important that the body obtains enough protein and calories from nutrient-dense foods to maintain energy and strength, and prevent body tissues from breaking down. Appetite is generally better in the morning. Clinical nutrition liquid meal replacements such as IMPACT® can be an easier solution when appetite is poor.

Many cancer patients are obese yet suffer from sarcopenia (muscle wasting). How to feed a 160+

Cancer Treatment	How it Can Affect Eating	What Sometimes Happens: Side Effects
Surgery	Increases the need for good nutrition. May slow digestion. May lessen the ability of the mouth, throat, and stomach to work properly. Adequate nutrition helps wound-healing and recovery.	Before surgery, a high-protein, high-calorie diet may be prescribed if a patient is underweight or weak. After surgery, some patients may not be able to eat normally at first. They may receive nutrients intravenously (such as in total parenteral nutrition), or through a tube in their nose or stomach.
Radiation Therapy	As it damages cancer cells, it also may affect healthy cells and healthy parts of the body.	Treatment of head, neck, chest, or breast may cause: • Dry mouth • Sore mouth • Sore throat • Difficulty swallowing • Change in taste of food • Dental problems • Increased phlegm Treatment of stomach or pelvis may cause: • Nausea and vomiting • Diarrhea • Cramps, bloating
Chemotherapy	As it destroys cancer cells, it also may affect the digestive system and the desire or ability to eat.	• Nausea and vomiting • Loss of appetite • Diarrhea • Constipation • Sore mouth or throat • Weight gain or loss • Change in taste of food
Biological Therapy (Immunotherapy)	As it stimulates your immune system to fight cancer cells, it can affect the desire or ability to eat.	• Nausea and vomiting • Diarrhea • Sore mouth • Severe weight loss • Dry mouth • Change in taste of food • Muscle aches, fatigue, fever
Hormonal Therapy	Some types can increase appetite and change how the body handles fluids.	• Changes in appetite • Fluid retention

Source: USNIH National Cancer Institute

kg cancer patient is still a problem. Specifically formulated products will need to be produced by industry to keep up with clinical requirements becoming evident today.

IMPACT®

Nestlé Nutrition recently acquired Novartis Medical Nutrition whose oral product **IMPACT®** is an advanced nutritional support solution for hospitalized patients. This product is clinically demonstrated to lower risk of infections by 30%, and can enable discharge from hospital an average of three days earlier than without it. IMPACT® promotes faster wound healing and a better general nutritional status for faster recovery. It is enriched with specific immune enhancing nutrients which scientific studies have shown to improve post-operative outcomes in patients undergoing surgery for gastrointestinal (GI) and head and neck malignancies. This product is an enteral sip and tube feed containing arginine, omega-3 fatty acids and nucleotides.

Arginine plays an important role in wound healing. Omega-3 fatty acids reduce the inflammatory response, favourably alter the production of cytokines, and are anti-thrombotic. Nucleotides are the building blocks of RNA and DNA. They support the development and activation of specialised immune cells during the immunological challenge represented by the disease, and maintain the integrity of bacterial cells. IMPACT® is the most widely studied product in the area of enteral nutrition with 26 studies showing supportive result, five published meta-analyses and five published economic analyses. Notably, fewer post-operative infectious complications such as wound infections, abdominal abscesses, urinary tract infections, and pneumonia are observed with the use of this product. In general IMPACT® complete nutrition is given five to seven days before surgery and continued for about a week afterwards. It is used under medical supervision and is available in citrus, tropical fruit and coffee flavours.

Some questions frequently raised in the media: Substances found in food and implications in carcinogenesis

Acrylamide

Polyacrylamide and acrylamide co-polymers are used in many industrial processes, including the treatment of drinking water, sewage and waste. They are also present in consumer products such as food packaging and some adhesives. Because acrylamide has been shown to cause cancer in laboratory rats when given in the animals' drinking water, both the Environmental Protection Agency (EPA) and the International Agency for Research on Cancer (IARC), consider acrylamide to be a potential human carcinogen. However, the relationship between acrylamide and cancer has not been clearly established in human beings. Probably formed during baking of starches at very high temperatures, it has been found in certain foods, with relatively high levels in potato crisps and French fries and lower levels in some breads and cereals. Food and cigarette smoke cause the greatest exposure to acrylamide, though some exposure may come from other sources. Neither regulatory bodies nor scientists have yet conclusively determined whether acrylamide in food poses a health risk for human beings.

Artificial Sweeteners

Questions about artificial sweeteners and cancer arose when studies in the early 1970s showed that high doses of ***Cyclamate*** in combination with ***Saccharin*** could cause bladder cancer in laboratory rats. However, results from subsequent carcinogenicity studies have not provided clear evidence of an association between artificial sweeteners and cancer in human beings. Because the bladder tumors seen in rats are due to a mechanism not relevant to humans, and because there is no clear evidence that saccharin causes cancer in humans, saccharin was delisted in 2000 from the U.S. National Toxicology Program's *Report on Carcinogens*, where it had been listed since 1981.

Aspartame was approved in 1981 by the FDA after numerous tests showed that it did not cause cancer or other adverse effects in laboratory animals. Questions regarding the safety of aspartame were renewed by a 1996 report suggesting that an increase in the number of people with brain tumours between 1975 and 1992 might be associated with the introduction and use of this sweetener in the United States. However, an analysis of statistics showed that the overall incidence of brain and central nervous system cancers began to rise in 1973, eight years ***before*** the approval of aspartame, and continued to rise until 1985. Moreover, increases in overall brain cancer incidence occurred primarily in people age 70 and older, a group that was not exposed to the highest doses of aspartame since its introduction. These data do not establish a clear link between the consumption of aspartame and the development of brain tumours.

Acesulfame K, ***Sucralose***, and ***Neotame*** are three other artificial sweeteners currently permitted for use in food. Acesulfame K was approved by the FDA in 1988 for use in certain food and beverage categories. Sucralose (also known as Splenda®) was approved by the FDA in 1998. Neotame, which is similar to aspartame, was approved in 2002. Before approving these sweeteners, the FDA reviewed more than 100 safety studies that were conducted on each sweetener, including studies to assess cancer risk. The results of these studies showed *no evidence* that these sweeteners cause cancer or pose any other threat to human health. Their advantage is they can replace sugars, which may be more closely associated with diabetes, obesity and cancer.

Food colourings

About 50 natural and artificial colour compounds are permitted for use in foods. The old azo dyes found to be carcinogenic in rat studies have long been removed from use. The colorants now regulated for use in food are judged by the UN and other expert committees as safe for use in foods and drinks. However, industry is listening to

consumer demand to remove artificial colourings, especially in children's foods. Consumers' fears have been raised by reports that illegal colourings may have been be used in some countries.

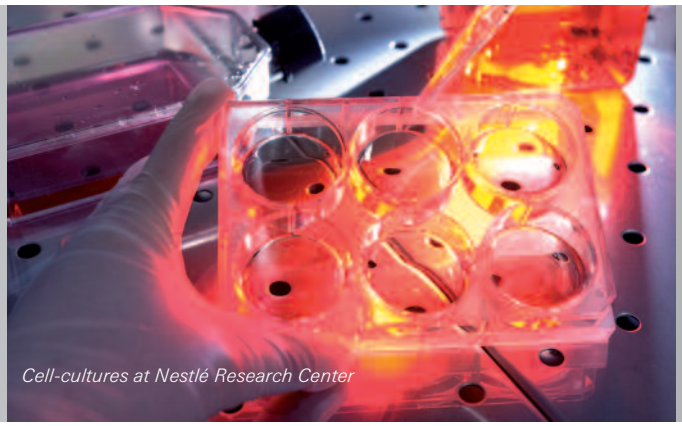
Heterocyclic amines in grilled meats

Research has shown that cooking certain meats at high temperatures creates chemicals that are not present in uncooked meats. Some of these chemicals may increase cancer risk. For example, heterocyclic amines (HCAs) are the carcinogenic chemicals formed during the cooking of meats such as beef, pork, fowl, and also fish. HCAs form when amino acids (the building blocks of proteins) and creatine (a chemical found in muscles) react at high cooking temperatures. Researchers have identified 17 different HCAs resulting from the cooking of meats that may pose human cancer risk. Research conducted by the National Cancer Institute (NCI) as well as by Japanese and European scientists indicates that heterocyclic amines are created within muscle meats during most types of high temperature cooking. Studies are being conducted to assess the amount of HCAs in the average diet, but at present the maximum daily intake of HCAs in food has not been firmly established.

Contaminants in drinking water

Bladder and liver cancer can be caused by contact with water contaminated by the schistomosome parasite's eggs. Populations living in areas without access to water chlorination are therefore at risk.

High concentrations of arsenic in drinking water have been found in areas of Bangladesh, China and West Bengal, and in more localised areas of Argentina, Australia, Chile, Mexico, Taiwan, China, Vietnam and the USA. In many of these regions, the drinking water is groundwater naturally tainted by arsenic-rich geological formations. The evidence that arsenic is a cause of lung cancer is convincing.



Cell-cultures at Nestlé Research Center

Nestlé Nutrition Symposium: Carcinogenesis, Cell Cycle and Therapeutics.

A short report on the Symposium is available from the Nestlé Nutrition Institute. www.nestle.nutrition-institute.org

This high level gathering included Nobel Prize winners who shared their findings on areas such as the complex cellular systems that maintain genomic stability, and new developments and insights gained over the past twenty years of cancer therapy.

The recognition of cellular mechanisms involved in cell damage and cancerous processes are being understood in ever greater detail. Diet can impact many of the biological targets involved in cell damage, and can additionally influence the protection and repair of molecules involved in cancer-related pathways. Today this knowledge is being used primarily to develop pharmaceutical therapies. However the group underlined the fact that cancer patients are in critical need of adequate nutrition, and that scientists and clinicians are currently working on the use of nutrition as a complement to therapies for improving their health.

Caring for Children with Cancer

Malnutrition and poor growth is frequent among children with cancer, due to an imbalance between intake and losses. When feeding child patients, the oral route is the preferred method, but when this is not possible, enteral nutrition (through the digestive tract) or parenteral (via the bloodstream) may be required. Enteral feeding is preferred over parenteral because it keeps the digestive tract working, and reduces the risk of infections. Its administration is safer and lessens the risk of complications in the bile function. Surprisingly, nasogastric tubing is well tolerated in children. Gastrostomy is also a useful method when correctly used and explained.

Special immuno-nutrition introduced before and after treatment procedures has made major progress over the last few years. Nutritional support can give the cancer patient a better chance when specialised diets are given at each stage of care.

Chronic Inflammation and Cancer

18% of human cancers (about 1.6 million per year) are related to infection. Infection can drive development of inflammation and so increase the production of free radicals which damage the DNA. It stimulates lipid peroxidation, ultimately driving cell proliferation. Chronic intestinal inflammation can progress to cancer of the colon. Inflammation, either leading to cancer or deriving from tumours themselves, is a leading area of pharmaceutical research. In nutrition, catechines from green tea and many other plant foods have been found to have an anti-inflammatory effect.

The Impact of Modern Biology on Cancer Treatment

The knowledge of molecular biology and genetics that is coming from basic science laboratories throughout the world is already having an influence on cancer treatment as it is on cancer detection and diagnosis.

Signal transduction is the complicated process by which growth signals are transmitted to the nucleus of the cell. Many efforts have been made to interfere specifically with that signalling. One such treatment has been highly successful in a chronic form of leukemia (for which it is now being used regularly) and is showing promise in other cancers.

Genetic Therapy As more is discovered about the molecular genetics of cancer, more advantage can be taken of specific genetic characteristics. For example, some patients with breast cancer have too many copies of a gene called *Her2/neu*. Scientists have been able to develop an antibody called trastuzumab *(Herceptin)* that is active against cancer in those patients. The fact that

specific defects can be related to individual kinds of cancer and that, in at least a few cases, can be turned into powerful, specific tools, provides promise that additional tools will be coming soon.

The Nestlé Research Center has joined forces with a team of companies and science institutes which will allow it to take advantage of new discoveries in the field of genomics. It is hoped that new breakthroughs in research, leading to cancer risk reduction, will result from such partnerships. The NRC has joined the industrial platform of the Kluyver Centre for Genomics of Industrial Fermentation, Netherlands. This platform consists of a variety of companies involved in the area of functional genomics and systems biology. Members of the group will benefit from direct access to results in bacterial genomics.

One aspect of the increasing use of genomics is expected to help support the potential benefits of probiotics by confirming their mechanism of action in the body. Chr Hansen in the past has been one of the firms already active in this area, using genomic tools to help it to investigate probiotic bacteria with superior benefits. Membership will also give access to the NRC to an extended network of scientists active in genomics and fermentation techniques using beneficial bacteria. This knowledge can be used for development of novel and better fermented food products such as yoghurts.

Other companies which are part of the platform include: Akzo Nobel Diosynth, Applikon, Bird Engineering, DSM, Friesland Foods, Heineken, Purac, Royal Nedalco and Tate & Lyle. Research at the Centre covers six programmes, including yeast, fungal and lactic acid fermentation, genomic tools and society, and genomics. Genomics is increasingly becoming a most exciting scientific tool in the area of nutrition, and it is hoped that nutrigenomics will be useful in the future for helping to prevent and treat a whole range of health problems, including obesity and cancer.

Gene therapy preparing culture dishes with gene corrected cells

What are the benefits to be expected from nutrition?

- ***Enhanced protection and prevention***
- ***Improved tolerance to treatment***
- ***Better therapeutic response***
- ***Improved quality of life***
- ***Enhanced survival***

To summarize:

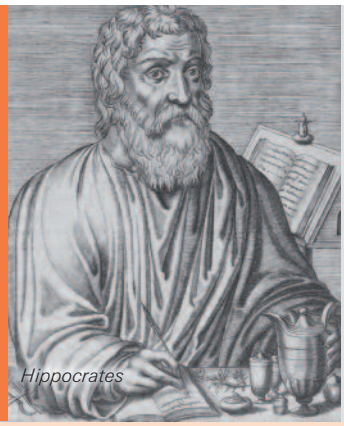
Cancer is a generic term describing more than 100 diseases that share the uncontrolled reproduction of abnormal cells. Because each cancer type is fundamentally different in origin, composition, and responsiveness to treatment, universal prevention techniques are exceedingly difficult to identify. It is difficult to demonstrate the benefit of preventive measures because of the long time the measures need to be in place before their results can be observed. Even if regular consumption of a food is shown to help reduce the risk of a certain type of cancer in a population group, there is no guarantee that eating or behaving in a certain way will absolutely assure freedom from cancer development in an individual.

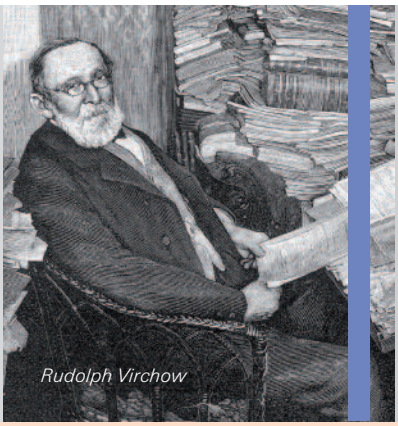
Much of the evidence for cancer prevention is not definitive. As an example, a diet low in fat but high in fibre, fruits and vegetables has been associated with lower risks in several cancer types. There have also been a number of studies that have shown no connection between these kinds of diets and lower rates of cancer. Exercise has shown positive influence on cancer occurrence in some studies; in others, exercise does not seem to make any difference.

Despite some conflicting evidence, the US National Cancer Institute contends that the best way to help prevent cancer is to exercise regularly, as well as eat a low calorie diet containing fibre, fruit, and vegetables. They suggest that people should avoid a sedentary lifestyle, stop smoking and avoid large quantities of animal fats and grilled meats. Research suggests that a balanced combination of different essential nutrients as opposed to a high level of one nutrient is the preferred approach to reduce cancer risk .

In closing the Nestlé Symposium, Professor Werner Bauer said that it was now very clear that the science of nutrition was re-emerging as one of the most exciting branches of the life sciences.

"Food is by far the largest molecular contact each of us has with our environment – the potential for food to play a role in modifying the risk and severity of cancer has to be an important one".


Hippocrates


Rudolph Virchow

Some Dates in the History of Cancer

Cancer is certainly not a disease of the modern industrialized age!

The oldest hominid malignant tumor was discovered in 1932 from the remains of either a *Homo erectus* or an *Australopithecus*. This tumor was suggestive of a Burkitt's lymphoma (although this nomenclature was not in use for the condition in the 1930s).

In 2698 BC the *Nei Ching*, the oldest treatise of medicine in China included the first descriptions of tumours and various forms of medical treatment including spiritual, medicinal, dietary and other recommendations.

In ancient Egypt, the oldest description of human cancer was found in a papyrus dated at around 1700 BC; a medical treatise containing descriptions of surgery, diagnosis, treatment and drugs. Cases of breast cancer documented by the early Egyptians were treated by cautery of the diseased tissue. Cancer was thought by the physicians and astrologers to be a punishment from the Gods. The treatment must certainly have certainly confirmed this impression on the sufferers. One of the earliest human cancers found in the remains of mummies was a bone cancer suggestive of osteosarcoma. The oldest specimen of a human cancer was found in the remains of a female skull dating back to the Bronze Age.

Some mummified skeletal remains of Peruvian Incas, dating back 2400 years, contained lesions suggestive of malignant melanoma.

In 460 BC was born ***Hippocrates***, the great, Greek father of western medicine. Hippocrates is credited with being the first to recognize the difference between benign and malignant tumors. His writings describe cancers of many body sites. He believed that an excess of black bile caused the disease. Legend has it that swollen blood vessels, like crab claws around the malignant tumors prompted him to name the disease *Karkinos (crab)* from which is derived our word cancer. But this explanation may be spurious.

The Roman ***Celsus***, 25BC described the four signs of inflammation (calor, rubor, dolor and turgor) and wrote his work *De Medicina* around 30AD in which he describes the fatty tumour atheroma.

In 1091 ***Avenzoar***, a physician of Moorish Spain, wrote in Arabic the *Kitab al Taisir fi al Mudawat wa al Tadbir* (Treatise of Medicine) which contained detailed descriptions of pathologies including tumours. ***Albucasis*** (1013–1106), of Cordoba, recommended an excision for early-stage cancers. If located in an accessible part: he recommended the cauterisation of the tissues around the area where the tumour was removed. As a pre-operative treatment, he purged the patient of his 'black bile' and bled him afterwards when his veins were 'inflated'.

In 1307 ***John of Arderne*** – an English surgeon was successful in treating abscesses. His main works were *Surgery* and the *Treatment of Anal Fistulas*. None of his cancer patients survived treatment however.

In 1443 ***Antonio Benivieni*** of Florence described the poor outcome of cancer of the stomach in his work *De Aditis Causis Morborum*.

1495 In the days of heroic surgery, excision of a gangrenous lung was carried out by ***Rolandus*** of Parma.

1580–1656 ***Marco Aurelio Severini*** described benign and malignant tumours of the breast with differential diagnoses. He illustrated his descriptions with drawings, and made clear descriptions of fibro-adenoma, advising the removal of benign tumours to avoid risk of degeneration.

By 1628, pathological autopsies by ***Harvey*** paved the way to better medical understanding. The discovery of the lymphatic system in the 17th Century provided further insight, but many erroneous theories circulated. In the 17th and 18th centuries, for example, some believed that cancer was contagious. In fact, the first cancer hospital in France was forced to delocate in 1779 because of the fear of the spread of cancer throughout the city. The lymph theory developed in the 17th century, replacing Hippocrates' black bile theory as a cause of cancer.

Wilhelm Conrad Roentgen

John Hill of London was the first to recognize the dangers of tobacco. In 1761, only a few decades after tobacco became popular in London, he wrote a book entitled *Cautions Against the Immoderate Use of Snuff*.

As the 19th Century was drawing to a close, a breakthrough came when ***Rudolph Virchow*** "the father of modern pathology" and ***Karl Thiersch*** recognized that cells derived from other cells, and that cancer spread through malignant cells. In 1896, another German, the physics professor ***Wilhelm Conrad Roentgen***, presented a remarkable lecture entitled "Concerning a New Kind of Ray." Roentgen called it the "x-ray", with "x" being the algebraic symbol for an unknown quantity. There was immediate worldwide enthusiasm. Within months, systems were being devised to use x-rays for diagnosis, and within three years radiation was used in the treatment of cancer. In 1901, Roentgen received the first Nobel Prize awarded for physics.

In 1926 a Nobel prize was awarded for the incorrect idea that stomach cancer was caused by a worm, but despite this shaky start, research progressed rapidly and continuously throughout the 20th Century. At the present time, some types of cancer can be cured, and much is understood about the disease.

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Nestlé

Good Food, Good Life

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