Epidemiologi Kanker

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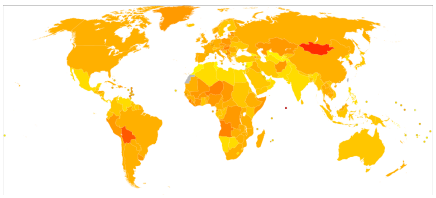
Epidemiology of cancer

The **epidemiology of cancer** is the study of the factors affecting cancer, as a way to infer possible trends and causes. The study of cancer epidemiology uses epidemiological methods to find the cause of cancer and to identify and develop improved treatments.



Death rate from cancer per 100,000 inhabitants in 2004. "WHO Disease and injury country estimates". World Health Organization. 2009. . Retrieved Nov. 11, 2009. no data less than 55 55–80 80–105 105–130 130–155 155–180 180–205 205–230 230–255 255–280 280–305 more than 305

This area of study must contend with problems of lead time bias and length time bias. Lead time bias is the concept that early diagnosis may artificially inflate the survival statistics of a cancer, without really improving the natural history of the disease. Length bias is the concept that slower growing, more indolent tumors are more likely to be diagnosed by screening tests, but improvements in diagnosing more cases of indolent cancer may not translate into better patient outcomes after the implementation of screening programs. A similar epidemiological concern is overdiagnosis, the tendency of screening tests to diagnose diseases that may not actually impact the patient's longevity. This problem especially applies to prostate cancer and PSA screening.[2]

Some cancer researchers have argued that negative cancer clinical trials lack sufficient statistical power to discover a benefit to treatment. This may be due to fewer patients enrolled in the study than originally planned.[3]

Organizations

State and regional cancer registries are organizations that abstract clinical data about cancer from patient medical records. These institutions provide information to state and national public health groups to help track trends in cancer diagnosis and treatment. One of the largest and most important cancer registries is Surveillance Epidemiology and End Results (SEER), administered by the US Federal government.[4] Health information privacy concerns have led to the restricted use of cancer registry data in the United States Department of Veterans Affairs[5][6][7] and other institutions.[8] The American Cancer Society predicts that approximately 1,690,000 new cancer cases will be diagnosed and 577,000 Americans will ultimately die of cancer in 2012.[9]

Studies

Observational epidemiological studies that show associations between risk factors and specific cancers mostly serve to generate hypotheses about potential interventions that could reduce cancer incidence or morbidity. Randomized controlled trials then test whether hypotheses generated by epidemiological studies and laboratory research actually result in reduced cancer incidence and mortality. In many cases, findings from observational epidemiological studies are not confirmed by randomized controlled trials.

Risk factors

The most significant risk factor is age. According to cancer researcher Robert A. Weinberg, "If we lived long enough, sooner or later we all would get cancer."[10] Essentially all of the increase in cancer rates between prehistoric times and people who died in England between 1901 and 1905 is due to increased lifespans.[10] Since then, some other factors, especially the increased use of tobacco, have further raised the rates.[10]

Over a third of cancer deaths worldwide are due to potentially modifiable risk factors. The leading modifiable risk factors worldwide are:

- tobacco smoking, which is strongly associated with lung cancer, mouth, and throat cancer;
- drinking alcohol, which is associated with a small increase in oral, esophageal, breast, and other cancers;
- a diet low in fruit and vegetables,
- physical inactivity, which is associated with increased risk of colon, breast, and possibly other cancers
- obesity, which is associated with colon, breast, endometrial, and possibly other cancers
- sexual transmission of human papillomavirus, which causes cervical cancer and some forms of anal cancer.

Men with cancer are twice as likely as women to have a modifiable risk factor for their disease.[11]

Other lifestyle and environmental factors known to affect cancer risk (either beneficially or detrimentally) include the use of exogenous hormones (e.g., hormone replacement therapy causes breast cancer), exposure to ionizing radiation and ultraviolet radiation, and certain occupational and chemical exposures.

Every year, at least 200,000 people die worldwide from cancer related to their workplace.[12] Millions of workers run the risk of developing cancers such as pleural and peritoneal mesothelioma from inhaling asbestos fibers, or leukemia from exposure to benzene at their workplaces.[12] Currently, most cancer deaths caused by occupational risk factors occur in the developed world.[12] It is estimated that approximately 20,000 cancer deaths and 40,000 new cases of cancer each year in the U.S. are attributable to occupation.[13]

Incidence and mortality

In the United States, cancer is responsible for 25% of all deaths with 30% of these from lung cancer. The most commonly occurring cancer in men is prostate cancer (about 25% of new cases) and in women is breast cancer (also about 25%). Cancer can occur in children and adolescents, but it is uncommon (about 150 cases per million in the U.S.), with leukemia the most common.[14] In the first year of life the incidence is about 230 cases per million in the U.S., with the most common being neuroblastoma.[15] Data from 2004-2008 in the United States indicates that the overall age-adjusted incidence of cancer was approximately 460 per 100,000 men and women per year.[16]

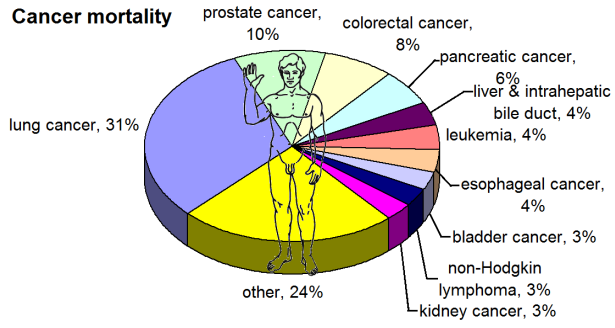
In the U.S. cancer is second only to cardiovascular disease as the leading cause of death;[14] in the UK it is the leading cause of death.[17] In many Third World countries cancer incidence (insofar as this can be measured) appears much lower, most likely because of the higher death rates due to infectious disease or injury. With the increased control over malaria and tuberculosis in some Third World countries, incidence of cancer is expected to rise; in the Eastern Mediterranean region, for example, cancer incidence is expected to increase by 100% to 180% in the next 15 years due to increases in life expectancy, an increasing proportion of elderly people, and the successful control of childhood disease.[18] This is termed the epidemiologic transition in epidemiological terminology.

In Canada, as of 2007, cancer is the number one cause of deaths contributing to 29.6% of all the demises in the country. The second highest cause of death is cardiovascular diseases resulting in 21.5% of deaths. Thus, cancer is a major disease affecting the population of Canada. As of 2011, the highest prevalence rate of cancer amongst males is prostate cancer (about 28% of all new cases) whereas in females its breast cancer (about 28% of all new cases). However, the leading cause of deaths with regards to both males and females is lung cancer which contributes to 26.8% of all deaths due to cancer. Statistics indicate that between the ages of 20 and 50 years, the incidence rate of cancer is higher amongst women whereas post 50 years of age, the incidence rate increases in men. Predictions by the Canadian Cancer Society indicate that with time, there will be an increase in the rates of incidence of cancer for

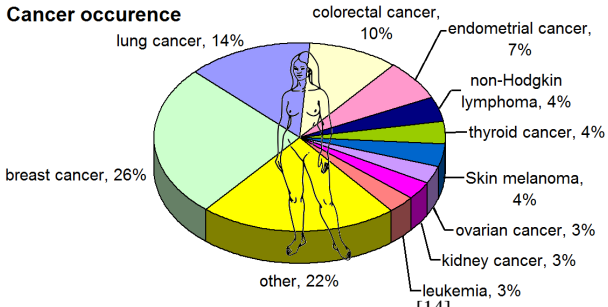
both males and females. This illustrates that cancer will continue to be a persistent issue over the next few years.

Cancer epidemiology closely mirrors risk factor spread in various countries. Hepatocellular carcinoma (liver cancer) is rare in the West but is the main cancer in China and neighbouring countries, most likely due to the endemic presence of hepatitis B and aflatoxin in that population. Similarly, with tobacco smoking becoming more common in various Third World countries, lung cancer incidence has increased in a parallel fashion.

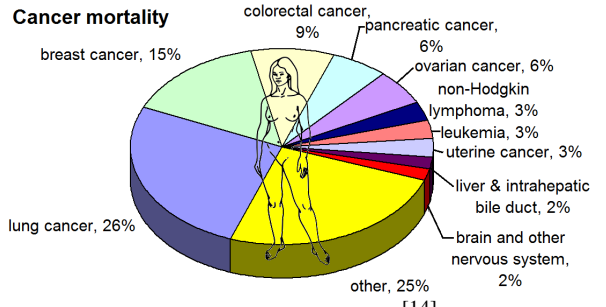
Cancer is responsible for about 25% of all deaths in the U.S., and is a major public health problem in many parts of the world. The statistics below are estimates for the U.S. in 2008, and may vary substantially in other countries. They exclude basal and squamous cell skin cancers, and carcinoma in situ in locations other than the urinary bladder.[14] As seen, breast/prostate cancer, lung cancer and colorectal cancer are responsible for approximately half of cancer incidence. The same applies for cancer mortality, but with lung cancer replacing breast/prostate cancer as the main cause.



in US males, by mortality[14]



in US females, by occurrence[14]



in US females, by mortality[14]

Male		Female	
most common (by occurrence)[14]	**most common (by mortality)[14]**	**most common (by occurrence)[14]**	**most common (by mortality)[14]**
prostate cancer (25%)	lung cancer (31%)	breast cancer (26%)	lung cancer (26%)
lung cancer (15%)	prostate cancer (10%)	lung cancer (14%)	breast cancer (15%)
colorectal cancer (10%)	colorectal cancer (8%)	colorectal cancer (10%)	colorectal cancer (9%)
bladder cancer (7%)	pancreatic cancer (6%)	endometrial cancer (7%)	pancreatic cancer (6%)

non-Hodgkin lymphoma (5%)	liver & intrahepatic bile duct (4%)	non-Hodgkin lymphoma (4%)	ovarian cancer (6%)
skin melanoma (5%)	leukemia (4%)	thyroid cancer (4%)	non-Hodgkin lymphoma (3%)
kidney cancer (4%)	esophageal cancer (4%)	Skin melanoma (4%)	leukemia (3%)
oral and pharyngeal cancer (3%)	bladder cancer (3%)	ovarian cancer (3%)	uterine cancer (3%)
leukemia (3%)	non-Hodgkin lymphoma (3%)	kidney cancer (3%)	liver & intrahepatic bile duct (2%)
pancreatic cancer (3%)	kidney cancer (3%)	leukemia (3%)	brain and other nervous system (2%)
other (20%)	other (24%)	other (22%)	other (25%)

Incidence of a second cancer in survivors

In the developed world, one in three people will develop cancer during their lifetimes. If all cancer patients survived and cancer occurred randomly, the normal lifetime odds of developing a second primary cancer (not the first cancer spreading to a new site) would be one in nine.[19] However, cancer survivors have an increased risk of developing a second primary cancer, and the odds are about two in nine.[19] About half of these second primaries can be attributed to the normal one-in-nine risk associated with random chance.[19] The increased risk is believed to be primarily due to the same risk factors that produced the first cancer, such as the person's genetic profile, alcohol and tobacco use, obesity, and environmental exposures, and partly due, in some cases, to the treatment for the first cancer, which might have included mutagenic chemotherapeutic drugs or radiation.[19] Cancer survivors may also be more likely to comply with recommended screening, and thus may be more likely than average to detect cancers.[19]

Children

Cancer can also occur in young children and adolescents, but it is rare (about 150 cases per million yearly in the US). Leukemia (usually acute lymphoblastic leukemia) is the most common cancer in children aged 1–14 in the U.S., followed by the central nervous system cancers, neuroblastoma, Wilms' tumor, and non-Hodgkin's lymphoma.[14] Statistics from the SEER program of the US NCI demonstrate that childhood cancers increased 19% between 1975 and 1990, mainly due to an increased incidence in acute leukemia. Since 1990, incidence rates have decreased.[20]

Infants

The age of peak incidence of cancer in children occurs during the first year of life, in infants. The average annual incidence in the United States, 1975–1995, was 233 per million infants.[20] Several estimates of incidence exist. According to SEER,[20] in the United States:

- Neuroblastoma comprised 28% of infant cancer cases and was the most common malignancy among these young children (65 per million infants).
- The leukemias as a group (41 per million infants) represented the next most common type of cancer, comprising 17% of all cases.
- Central nervous system malignancies comprised 13% of infant cancer, with an average annual incidence rate of nearly 30 per million infants.
- The average annual incidence rates for malignant germ cell and malignant soft tissue tumors were essentially the same at 15 per million infants. Each comprised about 6% of infant cancer.

Teratoma (a germ cell tumor) often is cited as the most common tumor in this age group, but most teratomas are surgically removed while still benign, hence not necessarily cancer. Prior to the widespread routine use of prenatal ultrasound examinations, the incidence of sacrococcygeal teratomas diagnosed at birth was 25 to 29 per million births.

Female and male infants have essentially the same overall cancer incidence rates, a notable difference compared to older children.

White infants have higher cancer rates than black infants. Leukemias accounted for a substantial proportion of this difference: the average annual rate for white infants (48.7 per million) was 66% higher than for black infants (29.4 per million).[20]

Relative survival for infants is very good for neuroblastoma, Wilms' tumor and retinoblastoma, and fairly good (80%) for leukemia, but not for most other types of cancer.

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External links

- CANCERMondial (http://www-dep.iarc.fr/)
- WHO/EMRO — GLOBOCAN (http://www.emro.who.int/ncd/cancer_globocan.htm)
- Cancer Epidemiology Resources (http://www.cancerindex.org/clinks4e.htm) — CancerIndex
- Surveillance, Epidemiology and End Results (http://seer.cancer.gov/) — National Cancer Institute

Diet and cancer

Diet and cancer are associated. While it is not yet possible to provide quantitative estimates of the overall risks, it has been estimated that 35 percent of cancer deaths may be related to dietary factors.[1] Almost all cancers (80–90%) are caused by environmental factors,[2] and of these, 30–40% of cancers are directly linked to the diet.[3] While many dietary recommendations have been proposed to reduce the risk of cancer, few have significant supporting scientific evidence.[4] The primary dietary factors that increase risk are obesity and alcohol consumption; with a diet low in fruits and vegetables and high in red meat being implicated but not confirmed.[5][6] Consumption of coffee is associated with a reduced risk of liver cancer.[7] Studies have linked consumption of red or processed meat to an increased risk of breast cancer, colon cancer, and pancreatic cancer, a phenomenon which could be due to the presence of carcinogens in foods cooked at high temperatures.[8][9] Thus dietary recommendation for cancer prevention typically include: "mainly vegetables, fruit, whole grain and fish and a reduced intake of red meat, animal fat and refined sugar."[4]

Fruits and vegetables

Fresh or frozen fruits and vegetables are both good, and contrary to common thought, frozen produce is just as nutrient dense as fresh produce, while dried produce is often sweetened, causing some of the nutrients to be broken down. Studies have shown produce consumption is effective in reducing cancers, especially in the gastrointestinal tract, lowering cancer rates by 22% and mortality to dietary related cancer by 11%.[10] Berries have been causing a lot of commotion and promise in the world of cancer research. The darker the berry, the better in terms of being more packed with nutrients that is better at warding off cancer. Research has been putting the spot light on black raspberries and their ability to reduce oxidative stress and gastroesophageal reflux disease, each of which causes damage to the esophageal cells.[11] Close runner-ups to the black raspberry are blueberries, blackberries, strawberries, and cranberries. These berries are high in vitamin C, fiber, and ellagic acid, which can prevent skin cancer.[12] In addition to these nutrients, the American Association for Cancer Research found that berries are extremely high in polyphenol phytochemicals, and some research is suggesting that these phytochemicals are what is inhibiting tumor growth, more so than vitamins and minerals. These phytochemicals have the ability to interfere with tumor development, probably due to their natural job of protecting plants and their structures, as well as maintaining their vibrant colors (2007). Beta-carotene and lycopene are two prevalent nutrients that have shown a lot of promise in their capabilities to slow tumor growth.[13]

Flavonoids

Flavonoids and catechins are nutrients that give foods a bitter taste, but they also are emerging as potential anticancer agents. The best sources are green and black teas, chocolate, wine, and grapes.[2] Catechins are a powerful form of antioxidant that act as a powerful inhibitor of cancer growth. In fact, catechins are 100 times more powerful than vitamin C and 25 times more powerful than vitamin E in their antioxidant/growth inhibitor powers. The flavonoids and catechins together have proven the ability to protect cells from x-ray damage, block the progression of the cell cycle, and inhibit mutations. Other foods high in flavonoids are garlic, onions, shallots, and leeks, which also contain vitamin C, selenium, and sulfur compounds that together, increase the metabolic disposal of chemical carcinogens,[2]

thus lowering the risk of cells turning cancerous.

Probiotics

Probiotics are bacteria that live in our gastrointestional tract and aid us in digestion as well as provide other benefits for its host. Ruize suggests that one of these benefits is their ability to eliminate procarcinogenic substances before they can turn carcinogenic. The probiotics are capable of altering certain enzymes (such as b-glucuronidase and nitro-reductase) that turn procarcinogens into carcinogenic agents by neutralizing the bad bacteria enzymes. Essentially, the good bacteria is cleansing the GI tract of harmful substances, such as poisonous bacteria and extraneous pollutants, found in the environment and our food chain. Without the probiotics, the immune system would be left to clean the body alone, causing a work overload and probably not as thorough, thus the probiotics are good because they help the immune system to keep toxins out of our intestines.[14] However, in a recent scientific study that was conducted in 2007 it was discovered that probiotics helped to prevent the development of preneoplastic lesions and tumors "in the colons of rats treated with chemical carcinogens,"[15] but in studies that were conducted with humans using the same procedure, methods, and variables that were used in the experiment with rats it was found that there was not an overwhelming amount of data that supported the claim that "probiotics exert[ed] protective effects against tumor development in the colon [of] [humans]."[15]

Reducing-risk factors

Increasing evidence suggests that diets high in foods containing fibre (or fiber) are associated with a reduced risk for cancer, especially cancer of the colon.[16]

A few studies have also shown a reduced risk for cancers of the breast, rectum, oral cavity, pharynx, stomach, and other sites with diets rich in fruits, vegetables and grain products.[17] Numerous studies have found evidence that carotenoids reduce the risk of some cancers. The evidence is particularly strong for lung cancer,[18] even after taking smoking into account. Vitamin C is found in fruits, particularly citrus fruits and juices, and in green vegetables, as well as in some fortified foods. Of a group of epidemiologic studies investigating the role of vitamin C, three-quarters found that vitamin C, or fruit rich in vitamin C, provides significant protection.[19]

A leaner diet is believed to lower cancer risk. Tomatoes, calcium, *agaricus blazei* mushrooms,[20] other minerals, saponins, sausage tree, sea mat, cat's claw, and licorice are believed to prevent or suppress different kinds of cancerous tumors. Furthermore, by eating a plant-based diet full of vegetables such as broccoli can prevent genes that cause cancer from being turned "on." A plant-based diet can prevent genes that cause cancer from being implemented and can also effect gene expression--manipulate genes.[21] Currently there is not enough evidence for using mushrooms or mushroom extracts in the treatment of cancer, but there is significant potential for research in the area and future clinical trials, due to the numerous scientific studies which have shown they may offer a beneficial effect.[22] Recently the diet of 34,192 Seventh-Day Adventists was studied and how their diets correlated to the development of colon and prostrate cancer. In the study the Seventh-Day Adventists that did not smoke or drink and were vegetarians reduced their risk of cancer, while Seventh-Day Adventists who consumed meat and neither smoke nor drank were more susceptible to developing cancer--people among their group who consumed beef regularly had a very high risk of developing bladder cancer.[23] Also, in the book *The China Study* it stipulates that there is a correlation that exists "between per capita meat and dairy consumption and prostate cancer mortality rate."[24]

Mushrooms

Some mushrooms offer an anti-cancer effect, which is thought to be linked to their ability to up-regulate the immune system. Some mushrooms known for this effect include, Reishi,[25][26] *Agaricus blazei*,[20] maitake,[27] and *Trametes versicolor*.[28] Research suggests the compounds in medicinal mushrooms most responsible for up-regulating the immune system and providing an anti-cancer effect, are a diverse collection of polysaccharide compounds, particularly beta-glucans. Beta-glucans are known as "biological response modifiers", and their ability to activate the immune system is well documented. Specifically, beta-glucans stimulate the innate branch of the immune system. Research has shown beta-glucans have the ability to stimulate macrophage, NK cells, T cells, and immune system cytokines. The mechanisms in which beta-glucans stimulate the immune system is only partially understood. One mechanism in which beta-glucans are able to activate the immune system, is by interacting with the Macrophage-1 antigen (CD18) receptor on immune cells.[29]

A highly purified compound isolated from the medicinal mushroom *Trametes versicolor*, known as Polysaccharide-K, has become incorporated into the health care system of a few countries, such as Japan.[30] Japan's Ministry of Health, Labour and Welfare approved the use of polysaccharide-K in the 1980s, to stimulate the immune systems of patients undergoing chemotherapy.

A recent study has identified verticillin A, isolated from *Verticillium* species-infected wild mushroom (*Amanita flavorubescens* Alk), as a potential anti-cancer agent.[31][32] When used in a high dose (i.e. 200 nM), verticillin A can directly kill cancer cells *in vitro*. The most interesting function of verticillin A is its ability to overcome apoptosis resistance of cancer cells when used in a lower dose (i.e. 10-20 nM). Verticillin A can dramatically increase metastatic human colon carcinoma cells to TRAIL- and FasL-induced apoptosis. Verticillin A regulates cell cycle and BNIP3 gene promoter DNA methylation to sensitze the tumor cells to apoptosis sensitization.[33]

Risk factors

Alcohol

Alcohol is a risk factor for cancers of the mouth, esophagus, pharynx, and larynx, breast cancer, colorectal cancer, and liver cancer.

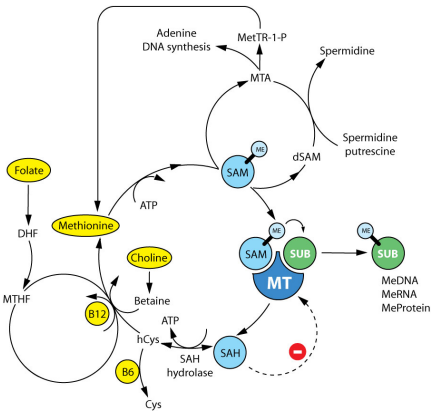
Contrary evidence

More recent studies have cast doubt on the claim that dietary fiber reduces the risk of colon cancer.[34][35] Regarding prostate cancer, a major 2002 study concluded that "A low-fat, high-fiber diet heavy in fruits and vegetables has no impact on PSA levels in men over a four-year period, and does not affect the incidence of prostate cancer."[36]

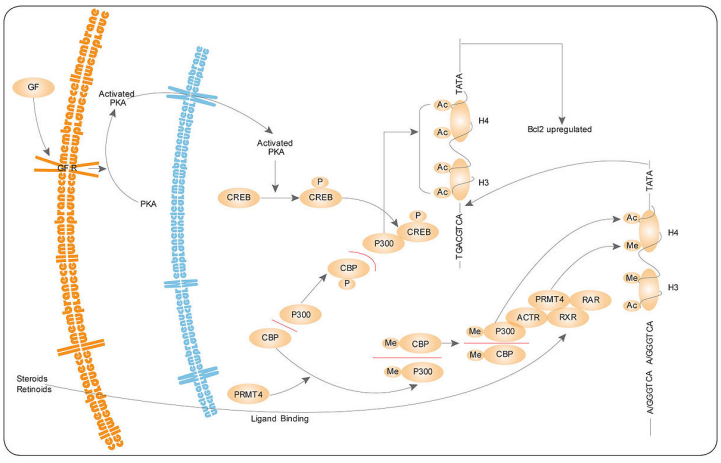
The belief that dietary fiber prevents these cancers was based on epidemiological evidence showing a very low incidence in the developing world. Dr. Denis Burkitt was the main proponent of this theory, and his 1979 best-selling book, "Don't Forget Fibre in Your Diet," was translated into nine languages. Less well-known is his theory, mentioned in the book, that the squatting defecation posture used in the developing world where Ottoman toilets are more widespread than the Western world is also a preventative factor, especially for colon diseases.

Methionine metabolism

Although numerous cellular mechanisms are involved in food intake, many investigations over the past decades have pointed out defects in the methionine metabolic pathway as cause of carcinogenesis.[37][38] For instance, deficiencies of the main dietary sources of methyl donors, methionine and choline, lead to the formation of liver cancer in rodents.[39][40] Methionine is an essential amino acid that must be provided by dietary intake of proteins or methyl donors (choline and betaine found in beef, eggs and some vegetables). Assimilated methionine is transformed in S-adenosyl methionine (SAM) which is a key metabolite for polyamine synthesis, e.g. spermidine, and cysteine formation (see the figure on the right). Methionine breakdown products are also recycled back into methionine by homocysteine remethylation and methylthioadenosine (MTA) conversion (see the figure on the right). Vitamins B_6, B_{12}, folic acid and choline are essential cofactors for these reactions. SAM is the substrate for methylation reactions catalyzed by DNA, RNA and protein methyltransferases.



The methionine metabolism pathway. DHF, dihydrofolate; dSAM, decarboxylated S-adenosylmethionine; hCys, homocysteine; ME, methyl group; MetTR-1-P, 5-methylthioribose-1-phosphate; MT, methyltransferase; MTA, methylthioadenosine; MTHF, methylenetetrahydrofolate; SAH, S-adenosyl-L-homocysteine; SAM, S-adenosyl methionine; SUB, substrate.



Growth factor (GF) and steroid/retinoid activation of PRMT4.

The products of these reactions are methylated DNA, RNA or proteins and S-adenosylhomocysteine (SAH). SAH has a negative feedback on its own production as an inhibitor of methyltransferase enzymes. Therefore SAM:SAH ratio directly regulates cellular methylation, whereas levels of vitamins B_6, B_{12}, folic acid and choline regulates indirectly the methylation state via the methionine metabolism cycle.[41][42] A near ubiquitous feature of cancer is a maladaption of the methionine metabolic pathway in response to genetic or environmental conditions resulting in depletion of SAM and/or SAM-dependent methylation. Whether it is deficiency in enzymes such as methylthioadenosine phosphorylase, methionine-dependency of cancer cells, high levels of polyamine synthesis in cancer, or induction of cancer through a diet deprived of extrinsic methyl donors or enhanced in methylation inhibitors, tumor formation is strongly correlated with a decrease in levels of SAM in mice, rats and humans.[43][44] Many indirect and thinly circumstantial theories have been put forth related to methylation status of DNA or attacks upon the capacity for DNA mutation and repair. The discovery that methyltransferases whose activity would be directly influenced by SAM levels also act as tumor suppressors potentially provides a more direct bridge. This has important ramifications for chemoprevention strategies as well as chemotherapy.[45][46][47][48]

Arginine methyltransferase

Protein arginine N-methyltransferase-4 (PRMT4) methylation of arginine residues within proteins plays a critical key role in transcriptional regulation (see the PRMT4 pathway on the left). PRMT4 binds to the classes of transcriptional activators known as p160 and CBP/p300.[49] The modified forms of these proteins are involved in stimulation of gene expression via steroid hormone receptors. Significantly, PRMT4 methylates core histones H3 and H4, which are also targets of the histone acetylase activity of CBP/p300 coactivators. PRMT4 recruitment chromatin by binding to coactivators increases histone methylation and enhances the accessibility of promoter regions for transcription. Methylation of the transcriptional coactivator CBP by PRMT4 inhibits binding to CREB and thereby partitions the limited cellular pool of CBP for steroid hormone receptor interaction.

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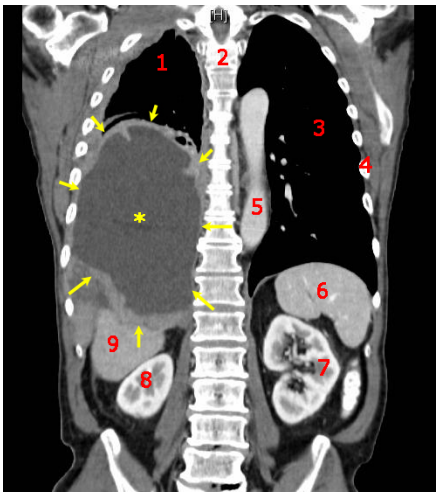
External links

- Food, Nutrition, Physical Activity and the Prevention of Cancer: a Global Perspective (http://www.dietandcancerreport.org/)
- Diet, healthy eating and cancer (http://info.cancerresearchuk.org/healthyliving/dietandhealthyeating/?a=5441)

Cancer

Cancer	
Classification and external resources	
 A coronal CT scan showing a malignant mesothelioma Legend: → tumor ←, ★ central pleural effusion, 1 & 3 lungs, 2 spine, 4 ribs, 5 aorta, 6 spleen, 7 & 8 kidneys, 9 liver.	
ICD-10	C00 [1]—C97 [2]
ICD-9	140 [3]—239 [4]
DiseasesDB	28843 [5]
MedlinePlus	001289 [6]
MeSH	D009369 [7]

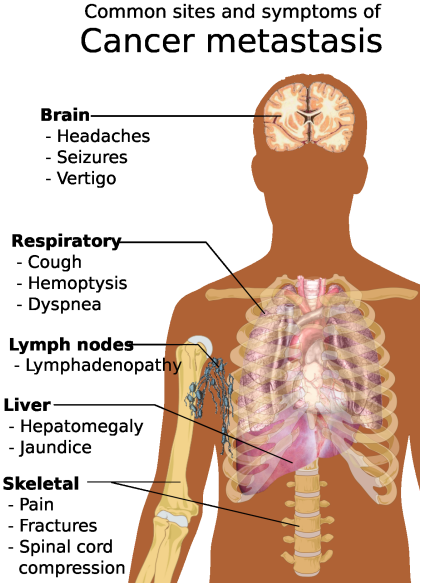
Cancer [i] /'kænsər/, known medically as a malignant neoplasm, is a broad group of various diseases, all involving unregulated cell growth. In cancer, cells divide and grow uncontrollably, forming malignant tumors, and invade nearby parts of the body. The cancer may also spread to more distant parts of the body through the lymphatic system or bloodstream. Not all tumors are cancerous. Benign tumors do not grow uncontrollably, do not invade neighboring tissues, and do not spread throughout the body. There are over 200 different known cancers that afflict humans.[8]

Determining what causes cancer is complex. Many things are known to increase the risk of cancer, including tobacco use, certain infections, radiation, lack of physical activity, obesity, and environmental pollutants.[9] These can directly damage genes or combine with existing genetic faults within cells to cause the disease.[10] Approximately five to ten percent of cancers are entirely hereditary.

Cancer can be detected in a number of ways, including the presence of certain signs and symptoms, screening tests, or medical imaging. Once a possible cancer is detected it is diagnosed by microscopic examination of a tissue sample. Cancer is usually treated with chemotherapy, radiation therapy and surgery. The chances of surviving the disease vary greatly by the type and location of the cancer and the extent of disease at the start of treatment. While cancer can affect people of all ages, and a few types of cancer are more common in children, the risk of developing cancer generally increases with age. In 2007, cancer caused about 13% of all human deaths worldwide (7.9 million). Rates are rising as more people live to an old age and as mass lifestyle changes occur in the developing world.[11]

Signs and symptoms

When cancer begins it invariably produces no symptoms with signs and symptoms only appearing as the mass continues to grow or ulcerates. The findings that result depends on the type and location of the cancer. Few symptoms are specific, with many of them also frequently occurring in individuals who have other conditions. Cancer is the new "great imitator". Thus it is not uncommon for people diagnosed with cancer to have been treated for other diseases to which it was assumed their symptoms were due.[12]



Symptoms of cancer metastasis depend on the location of the tumor.

Local effects

Local symptoms may occur due to the mass of the tumor or its ulceration. For example mass effects from lung cancer can cause blockage of the bronchus resulting in cough or pneumonia, esophageal cancer can cause narrowing of the esophagus making it difficult or painful to swallow, and colorectal cancer may lead to narrowing or blockages in the bowel resulting in changes in bowel habits. Masses of breast or testicles may be easily felt. Ulceration can cause bleeding which, if it occurs in the lung, will lead to coughing up blood, in the bowels to anemia or rectal bleeding, in the bladder to blood in the urine, and in the uterus to vaginal bleeding. Although localized pain may occur in advanced cancer, the initial swelling is usually painless. Some cancers can cause build up of fluid within the chest or abdomen.[12]

Systemic symptoms

General symptoms occur due to distant effects of the cancer that are not related to direct or metastatic spread. These may include: unintentional weight loss, fever, being excessively tired, and changes to the skin.[13] Hodgkin disease, leukemias, and cancers of the liver or kidney can cause a persistent fever of unknown origin.[12]

Specific constellations of systemic symptoms, termed paraneoplastic phenomena, may occur with some cancers. Examples include the appearance of myasthenia gravis in thymoma and clubbing in lung cancer.[12]

Metastasis

Symptoms of metastasis are due to the spread of cancer to other locations in the body. They can include enlarged lymph nodes (which can be felt or sometimes seen under the skin and are typically hard), hepatomegaly (enlarged liver) or splenomegaly (enlarged spleen) which can be felt in the abdomen, pain or fracture of affected bones, and neurological symptoms.[12]

Causes

Cancers are primarily an environmental disease with 90-95% of cases attributed to environmental factors and 5-10% due to genetics.[9] *Environmental*, as used by cancer researchers, means any cause that is not inherited genetically, not merely pollution.[14] Common environmental factors that contribute to cancer death include tobacco (25-30%), diet and obesity (30-35%), infections (15-20%), radiation (both ionizing and non-ionizing, up to 10%), stress, lack of physical activity, and environmental pollutants.[9]

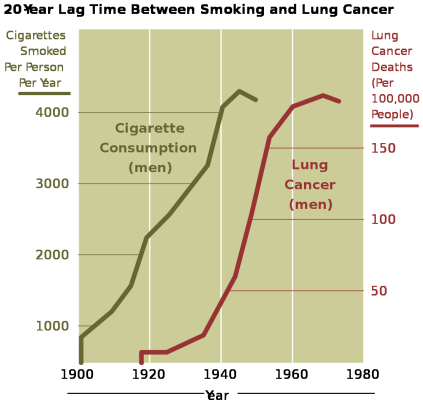
It is nearly impossible to prove what caused a cancer in any individual, because most cancers have multiple possible causes. For example, if a person who uses tobacco heavily develops lung cancer, then it was probably caused by the

tobacco use, but since everyone has a small chance of developing lung cancer as a result of air pollution or radiation, then there is a small chance that the cancer developed because of air pollution or radiation.

Chemicals

Further information: Alcohol and cancer and Smoking and cancer

Cancer pathogenesis is traceable back to DNA mutations that impact cell growth and metastasis. Substances that cause DNA mutations are known as mutagens, and mutagens that cause cancers are known as carcinogens. Particular substances have been linked to specific types of cancer. Tobacco smoking is associated with many forms of cancer,[15] and causes 90% of lung cancer.[16]



The incidence of lung cancer is highly correlated with smoking.

Many mutagens are also carcinogens, but some carcinogens are not mutagens. Alcohol is an example of a chemical carcinogen that is not a mutagen.[17] In Western Europe 10% of cancers in males and 3% of cancers in females are attributed to alcohol.[18]

Decades of research has demonstrated the link between tobacco use and cancer in the lung, larynx, head, neck, stomach, bladder, kidney, esophagus and pancreas.[19] Tobacco smoke contains over fifty known carcinogens, including nitrosamines and polycyclic aromatic hydrocarbons.[20] Tobacco is responsible for about one in three of all cancer deaths in the developed world,[15] and about one in five worldwide.[20] Lung cancer death rates in the United States have mirrored smoking patterns, with increases in smoking followed by dramatic increases in lung cancer death rates and, more recently, decreases in smoking rates since the 1950s followed by decreases in lung cancer death rates in men since 1990.[21][22] However, the numbers of smokers worldwide is still rising, leading to what some organizations have described as the *tobacco epidemic*.[23]

Cancer related to one's occupation is believed to represent between 2–20% of all cases.[24] Every year, at least 200,000 people die worldwide from cancer related to their workplace.[25] Most cancer deaths caused by occupational risk factors occur in the developed world.[25] It is estimated that approximately 20,000 cancer deaths and 40,000 new cases of cancer each year in the U.S. are attributable to occupation.[26] Millions of workers run the risk of developing cancers such as lung cancer and mesothelioma from inhaling asbestos fibers and tobacco smoke, or leukemia from exposure to benzene at their workplaces.[25]

Diet and exercise

Diet, physical inactivity, and obesity are related to approximately 30–35% of cancer deaths.[9][27] In the United States excess body weight is associated with the development of many types of cancer and is a factor in 14–20% of all cancer deaths.[27] Physical inactivity is believed to contribute to cancer risk not only through its effect on body weight but also through negative effects on immune system and endocrine system.[27]

Diets that are low in vegetables, fruits and whole grains, and high in processed or red meats are linked with a number of cancers.[27] A high salt diet is linked to gastric cancer, aflatoxin B1, a frequent food contaminate, with liver cancer, and Betel nut chewing with oral cancer.[28] This may partly explain differences in cancer incidence in different countries for example gastric cancer is more common in Japan with its high salt diet[29] and colon cancer is more common in the United States. Immigrants develop the risk of their new country, often within one generation, suggesting a substantial link between diet and cancer.[30]

Infection

Worldwide approximately 18% of cancer deaths are related to infectious diseases.[9] This proportion varies in different regions of the world from a high of 25% in Africa to less than 10% in the developed world.[9] Viruses are the usual infectious agents that cause cancer but bacteria and parasites may also have an effect.

A virus that can cause cancer is called an *oncovirus*. These include human papillomavirus (cervical carcinoma), Epstein-Barr virus (B-cell lymphoproliferative disease and nasopharyngeal carcinoma), Kaposi's sarcoma herpesvirus (Kaposi's Sarcoma and primary effusion lymphomas), hepatitis B and hepatitis C viruses (hepatocellular carcinoma), and Human T-cell leukemia virus-1 (T-cell leukemias). Bacterial infection may also increase the risk of cancer, as seen in Helicobacter pylori-induced gastric carcinoma.[31] Parasitic infections strongly associated with cancer include *Schistosoma haematobium* (squamous cell carcinoma of the bladder) and the liver flukes, *Opisthorchis viverrini* and *Clonorchis sinensis* (cholangiocarcinoma).[32]

Radiation

Up to 10% of invasive cancers are related to radiation exposure, including both ionizing radiation and non-ionizing radiation.[9] Additionally, the vast majority of non-invasive cancers are non-melanoma skin cancers caused by non-ionizing ultraviolet radiation.

Sources of ionizing radiation include medical imaging, and radon gas. Radiation can cause cancer in most parts of the body, in all animals, and at any age, although radiation-induced solid tumors usually take 10–15 years, and can take up to 40 years, to become clinically manifest, and radiation-induced leukemias typically require 2–10 years to appear.[33] Some people, such as those with nevoid basal cell carcinoma syndrome or retinoblastoma, are more susceptible than average to developing cancer from radiation exposure.[33] Children and adolescents are twice as likely to develop radiation-induced leukemia as adults; radiation exposure before birth has ten times the effect.[33] Ionizing radiation is not a particularly strong mutagen.[33] Residential exposure to radon gas, for example, has similar cancer risks as passive smoking.[33] Low-dose exposures, such as living near a nuclear power plant, are generally believed to have no or very little effect on cancer development.[33] Radiation is a more potent source of cancer when it is combined with other cancer-causing agents, such as radon gas exposure plus smoking tobacco.[33]

Unlike chemical or physical triggers for cancer, ionizing radiation hits molecules within cells randomly. If it happens to strike a chromosome, it can break the chromosome, result in an abnormal number of chromosomes, inactivate one or more genes in the part of the chromosome that it hit, delete parts of the DNA sequence, cause chromosome translocations, or cause other types of chromosome abnormalities.[33] Major damage normally results in the cell dying, but smaller damage may leave a stable, partly functional cell that may be capable of proliferating and developing into cancer, especially if tumor suppressor genes were damaged by the radiation.[33] Three independent stages appear to be involved in the creation of cancer with ionizing radiation: morphological changes to the cell, acquiring cellular immortality (losing normal, life-limiting cell regulatory processes), and adaptations that favor formation of a tumor.[33] Even if the radiation particle does not strike the DNA directly, it triggers responses from cells that indirectly increase the likelihood of mutations.[33]

Medical use of ionizing radiation is a growing source of radiation-induced cancers. Ionizing radiation may be used to treat other cancers, but this may, in some cases, induce a second form of cancer.[33] It is also used in some kinds of medical imaging. One report estimates that approximately 29,000 future cancers could be related to the approximately 70 million CT scans performed in the US in 2007.[34] It is estimated that 0.4% of cancers in 2007 in the United States are due to CTs performed in the past and that this may increase to as high as 1.5–2% with rates of CT usage during this same time period.[35]

Prolonged exposure to ultraviolet radiation from the sun can lead to melanoma and other skin malignancies.[36] Clear evidence establishes ultraviolet radiation, especially the non-ionizing medium wave UVB, as the cause of most non-melanoma skin cancers, which are the most common forms of cancer in the world.[36]

Non-ionizing radio frequency radiation from mobile phones, electric power transmission, and other similar sources have been described as a possible carcinogen by the World Health Organization's International Agency for Research on Cancer.[37]

Heredity

The vast majority of cancers are non-hereditary ("sporadic cancers"). Hereditary cancers are primarily caused by an inherited genetic defect. Less than 0.3% of the population are carriers of a genetic mutation which has a large effect on cancer risk and these cause less than 3–10% of all cancer.[38] Some of these syndromes include: certain inherited mutations in the genes *BRCA1* and *BRCA2* with a more than 75% risk of breast cancer and ovarian cancer,[38] and hereditary nonpolyposis colorectal cancer (HNPCC or Lynch syndrome) which is present in about 3% of people with colorectal cancer,[39] among others.

Physical agents

Some substances cause cancer primarily through their physical, rather than chemical, effects on cells.[40]

A prominent example of this is prolonged exposure to asbestos, naturally occurring mineral fibers which are a major cause of mesothelioma, a type of lung cancer.[40] Other substances in this category, including both naturally occurring and synthetic asbestos-like fibers such as wollastonite, attapulgite, glass wool, and rock wool, are believed to have similar effects.[40]

Nonfibrous particulate materials that cause cancer include powdered metallic cobalt and nickel, and crystalline silica (quartz, cristobalite, and tridymite).[40]

Usually, physical carcinogens must get inside the body (such as through inhaling tiny pieces) and require years of exposure to develop cancer.[40]

Physical trauma resulting in cancer is relatively rare.[41] Claims that breaking bone resulted in bone cancer, for example, have never been proven.[41] Similarly, physical trauma is not accepted as a cause for cervical cancer, breast cancer, or brain cancer.[41]

One accepted source is frequent, long-term application of hot objects to the body. It is possible that repeated burns on the same part of the body, such as those produced by kanger and kairo heaters (charcoal hand warmers), may produce skin cancer, especially if carcinogenic chemicals are also present.[41] Frequently drinking scalding hot tea may produce esophageal cancer.[41]

Generally, it is believed that the cancer arises, or a pre-existing cancer is encouraged, during the process of repairing the trauma, rather than the cancer being caused directly by the trauma.[41] However, repeated injuries to the same tissues might promote excessive cell proliferation, which could then increase the odds of a cancerous mutation. There is no evidence that inflammation itself causes cancer.[41]

Hormones

Some hormones play a role in the development of cancer by promoting cell proliferation.[42] Hormones are important agents in sex-related cancers such as cancer of the breast, endometrium, prostate, ovary, and testis, and also of thyroid cancer and bone cancer.[42]

An individual's hormone levels are mostly determined genetically, so this may at least partly explains the presence of some cancers that run in families that do not seem to have any cancer-causing genes.[42] For example, the daughters of women who have breast cancer have significantly higher levels of estrogen and progesterone than the daughters of women without breast cancer. These higher hormone levels may explain why these women have higher risk of breast cancer, even in the absence of a breast-cancer gene.[42] Similarly, men of African ancestry have significantly higher levels of testosterone than men of European ancestry, and have a correspondingly much higher level of prostate cancer.[42] Men of Asian ancestry, with the lowest levels of testosterone-activating androstanediol glucuronide, have

the lowest levels of prostate cancer.[42]

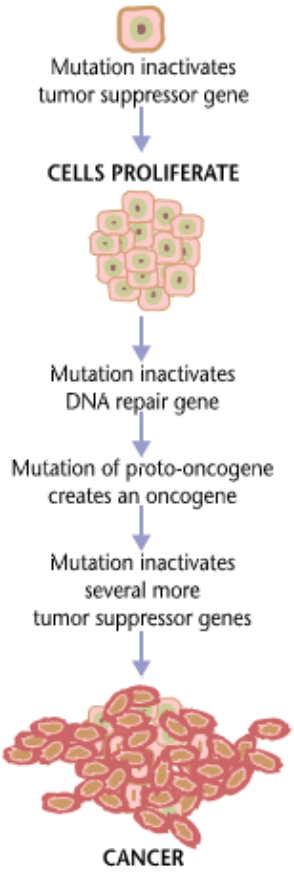
However, non-genetic factors are also relevant: obese people have higher levels of some hormones associated with cancer and a higher rate of those cancers.[42] Women who take hormone replacement therapy have a higher risk of developing cancers associated with those hormones.[42] On the other hand, people who exercise far more than average have lower levels of these hormones, and lower risk of cancer.[42] Osteosarcoma may be promoted by growth hormones.[42] Some treatments and prevention approaches leverage this cause by artificially reducing hormone levels, and thus discouraging hormone-sensitive cancers.[42]

Other

Excepting the rare transmissions that occur with pregnancies and only a marginal few organ donors, cancer is generally not a transmissible disease. The main reason for this is tissue graft rejection caused by MHC incompatibility.[43] In humans and other vertebrates, the immune system uses MHC antigens to differentiate between "self" and "non-self" cells because these antigens are different from person to person. When non-self antigens are encountered, the immune system reacts against the appropriate cell. Such reactions may protect against tumour cell engraftment by eliminating implanted cells. In the United States, approximately 3,500 pregnant women have a malignancy annually, and transplacental transmission of acute leukaemia, lymphoma, melanoma and carcinoma from mother to fetus has been observed.[43] The development of donor-derived tumors from organ transplants is exceedingly rare. The main cause of organ transplant associated tumors seems to be malignant melanoma, that was undetected at the time of organ harvest.[44] Cancer from one organism will usually grow in another organism of that species, as long as they share the same histocompatibility genes,[45] proven using mice; however this would never happen in a real-world setting except as described above.

In non-humans, a few types of transmissible cancer have been described, wherein the cancer spreads between animals by transmission of the tumor cells themselves. This phenomenon is seen in dogs with Sticker's sarcoma, also known as canine transmissible venereal tumor,[46] as well as devil facial tumour disease in Tasmanian devils.

Pathophysiology



Cancers are caused by a series of mutations. Each mutation alters the behavior of the cell somewhat.

Cancer is fundamentally a disease of failure of regulation of tissue growth. In order for a normal cell to transform into a cancer cell, the genes which regulate cell growth and differentiation must be altered.[47]

The affected genes are divided into two broad categories. Oncogenes are genes which promote cell growth and reproduction. Tumor suppressor genes are genes which inhibit cell division and survival. Malignant transformation can occur through the formation of novel oncogenes, the inappropriate over-expression of normal oncogenes, or by the under-expression or disabling of tumor suppressor genes. Typically, changes in *many* genes are required to transform a normal cell into a cancer cell.[48]

Genetic changes can occur at different levels and by different mechanisms. The gain or loss of an entire chromosome can occur through errors in mitosis. More common are mutations, which are changes in the nucleotide sequence of genomic DNA.

Large-scale mutations involve the deletion or gain of a portion of a chromosome. Genomic amplification occurs when a cell gains many copies (often 20 or more) of a small chromosomal locus, usually containing one or more oncogenes and adjacent genetic material. Translocation occurs when two separate chromosomal regions become abnormally fused, often at a characteristic location. A well-known example of this is the Philadelphia chromosome, or translocation of chromosomes 9 and 22, which occurs in chronic myelogenous leukemia, and results in production of the BCR-abl fusion protein, an oncogenic tyrosine kinase.

Small-scale mutations include point mutations, deletions, and insertions, which may occur in the promoter region of a gene and affect its expression, or may occur in the gene's coding sequence and alter the function or stability of its protein product. Disruption of a single gene may also result from integration of genomic material from a DNA virus or retrovirus, and resulting in the expression of *viral* oncogenes in the affected cell and its descendants.

Replication of the enormous amount of data contained within the DNA of living cells will probabilistically result in some errors (mutations). Complex error correction and prevention is built into the process, and safeguards the cell against cancer. If significant error occurs, the damaged cell can "self-destruct" through programmed cell death, termed apoptosis. If the error control processes fail, then the mutations will survive and be passed along to daughter cells.

Some environments make errors more likely to arise and propagate. Such environments can include the presence of disruptive substances called carcinogens, repeated physical injury, heat, ionising radiation, or hypoxia[49]

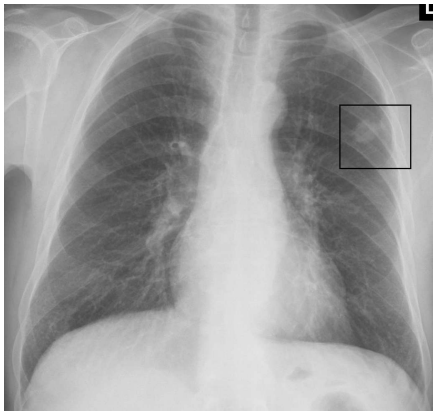
The errors which cause cancer are *self-amplifying* and *compounding*, for example:

- A mutation in the error-correcting machinery of a cell might cause that cell and its children to accumulate errors more rapidly.
- A further mutation in an oncogene might cause the cell to reproduce more rapidly and more frequently than its normal counterparts.
- A further mutation may cause loss of a tumour suppressor gene, disrupting the apoptosis signalling pathway and resulting in the cell becoming immortal.
- A further mutation in signaling machinery of the cell might send error-causing signals to nearby cells.

The transformation of normal cell into cancer is akin to a chain reaction caused by initial errors, which compound into more severe errors, each progressively allowing the cell to escape the controls that limit normal tissue growth. This rebellion-like scenario becomes an undesirable survival of the fittest, where the driving forces of evolution work against the body's design and enforcement of order. Once cancer has begun to develop, this ongoing process, termed *clonal evolution* drives progression towards more invasive stages.[50]

Diagnosis

Most cancers are initially recognized either because of the appearance of signs or symptoms or through screening. Neither of these lead to a definitive diagnosis, which requires the examination of a tissue sample by a pathologist. People with suspected cancer are investigated with medical tests. These commonly include blood tests, X-rays, CT scans and endoscopy.



Chest x-ray showing lung cancer in the left lung.

Classification

Cancers are classified by the type of cell that the tumor cells resemble and is therefore presumed to be the origin of the tumor. These types include:

- Carcinoma: Cancers derived from epithelial cells. This group includes many of the most common cancers, particularly in the aged, and include nearly all those developing in the breast, prostate, lung, pancreas, and colon.
- Sarcoma: Cancers arising from connective tissue (i.e. bone, cartilage, fat, nerve), each of which develop from cells originating in mesenchymal cells outside the bone marrow.
- Lymphoma and leukemia: These two classes of cancer arise from hematopoietic (blood-forming) cells that leave the marrow and tend to mature in the lymph nodes and blood, respectively. Leukemia is the most common type of cancer in children accounting for about 30%.[51]
- Germ cell tumor: Cancers derived from pluripotent cells, most often presenting in the testicle or the ovary (seminoma and dysgerminoma, respectively).
- Blastoma: Cancers derived from immature "precursor" cells or embryonic tissue. Blastomas are more common in children than in older adults.

Cancers are usually named using *-carcinoma*, *-sarcoma* or *-blastoma* as a suffix, with the Latin or Greek word for the organ or tissue of origin as the root. For example, cancers of the liver parenchyma arising from malignant epithelial cells is called *hepatocarcinoma*, while a malignancy arising from primitive liver precursor cells is called a hepatoblastoma, and a cancer arising from fat cells is called a *liposarcoma*. For some common cancers, the English organ name is used. For example, the most common type of breast cancer is called *ductal carcinoma of the breast*. Here, the adjective *ductal* refers to the appearance of the cancer under the microscope, which suggests that it has originated in the milk ducts.

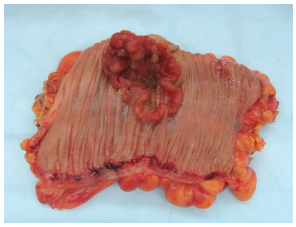
Benign tumors (which are not cancers) are named using *-oma* as a suffix with the organ name as the root. For example, a benign tumor of smooth muscle cells is called a *leiomyoma* (the common name of this frequently occurring benign tumor in the uterus is *fibroid*). Confusingly, some types of cancer also use the *-oma* suffix, examples including melanoma and seminoma.

Some types of cancer are named for the size and shape of the cells under a microscope, such as giant cell carcinoma, spindle cell carcinoma, and small cell carcinoma.

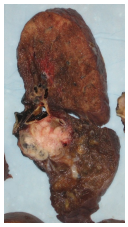
Pathology

The tissue diagnosis given by the pathologist indicates the type of cell that is proliferating, its histological grade, genetic abnormalities, and other features of the tumor. Together, this information is useful to evaluate the prognosis of the patient and to choose the best treatment. Cytogenetics and immunohistochemistry are other types of testing that the pathologist may perform on the tissue specimen. These tests may provide information about the molecular changes (such as mutations, fusion genes, and numerical chromosome changes) that has happened in the cancer cells, and may thus also indicate the future behavior of the cancer (prognosis) and best treatment.

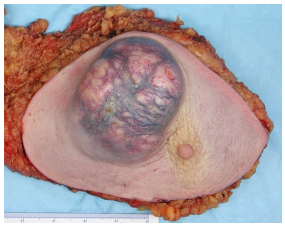
An invasive ductal carcinoma of the breast (pale area at the center) surrounded by spikes of whitish scar tissue and yellow fatty tissue.



An invasive colorectal carcinoma (top center) in a colectomy specimen.



A squamous cell carcinoma (the whitish tumor) near the bronchi in a lung specimen.



A large invasive ductal carcinoma in a mastectomy specimen.

Prevention

Cancer prevention is defined as active measures to decrease the risk of cancer.[52] The vast majority of cancer risk factors are due to environmental (including lifestyle) factors, and many of these factors are controllable. Thus, cancer is largely considered a preventable disease.[53] Greater than 30% of cancer is considered preventable by avoiding risk factors including: tobacco, overweight / obesity, an insufficient diet, physical inactivity, alcohol, sexually transmitted infections, and air pollution.[54] Not all environmental causes can be prevented completely such as naturally occurring background radiation.

Dietary

While many dietary recommendations have been proposed to reduce the risk of cancer, few have significant supporting scientific evidence.[55] The primary dietary factors that increase risk are obesity and alcohol consumption; with a diet low in fruits and vegetables and high in red meat being implicated but not confirmed.[56][57] Consumption of coffee is associated with a reduced risk of liver cancer.[58]Studies have linked consumption of red or processed meat to an increased risk of breast cancer, colon cancer, and pancreatic cancer, a phenomenon which could be due to the presence of carcinogens in foods cooked at high temperatures.[59][60] Thus dietary recommendation for cancer prevention typically include: "mainly vegetables, fruit, whole grain and fish and a reduced intake of red meat, animal fat and refined sugar."[55]

Medication

The concept that medications can be used to prevent cancer is attractive, and evidence supports their use in a few defined circumstances.[61] In the general population NSAIDs reduce the risk of colorectal cancer however due to the cardiovascular and gastrointestinal side effects they cause overall harm when used for prevention.[62] Aspirin has been found to reduce the risk of death from cancer by about 7%.[63] COX-2 inhibitor may decrease the rate of polyp formation in people with familial adenomatous polyposis however are associated with the same adverse effects as

NSAIDs.[64] Daily use of tamoxifen or raloxifene has been demonstrated to reduce the risk of developing breast cancer in high-risk women.[65] The benefit verses harm for 5-alpha-reductase inhibitor such as finasteride is not clear.[66]

Vitamins have not been found to be effective at preventing cancer,[67] although low blood levels of vitamin D are correlated with increased cancer risk.[68][69] Whether this relationship is causal and vitamin D supplementation is protective is not determined.[70] Beta-carotene supplementation has been found to increase lung cancer rates in those who are high risk.[71] Folic acid supplementation has not been found effective in preventing colon cancer and may increase colon polyps.[72]

Vaccination

Vaccines have been developed that prevent some infection by some viruses.[73] Human papillomavirus vaccine (Gardasil and Cervarix) decreases the risk of developing cervical cancer.[73] The hepatitis B vaccine prevents infection with hepatitis B virus and thus decreases the risk of liver cancer.[73]

Screening

Unlike diagnosis efforts prompted by symptoms and medical signs, cancer screening involves efforts to detect cancer after it has formed, but before any noticeable symptoms appear.[74] This may involve physical examination, blood or urine tests, or medical imaging.[74]

Cancer screening is currently not possible for many types of cancers, and even when tests are available, they may not be recommended for everyone. *Universal screening* or *mass screening* involves screening everyone.[75] *Selective screening* identifies people who are known to be at higher risk of developing cancer, such as people with a family history of cancer.[75] Several factors are considered to determine whether the benefits of screening outweigh the risks and the costs of screening.[74] These factors include:

- Possible harms from the screening test: for example, X-ray images involve exposure to potentially harmful ionizing radiation.
- The likelihood of the test correctly identifying cancer.
- The likelihood of cancer being present: Screening is not normally useful for rare cancers.
- Possible harms from follow-up procedures.
- Whether suitable treatment is available.
- Whether early detection improves treatment outcomes.
- Whether the cancer will ever need treatment.
- Whether the test is acceptable to the people: If a screening test is too burdensome (for example, being extremely painful), then people will refuse to participate.[75]
- Cost of the test.

Recommendations

The U.S. Preventive Services Task Force (USPSTF) strongly recommends cervical cancer screening in women who are sexually active and have a cervix at least until the age of 65.[76] They recommend that Americans be screened for colorectal cancer via fecal occult blood testing, sigmoidoscopy, or colonoscopy starting at age 50 until age 75.[77] There is insufficient evidence to recommend for or against screening for skin cancer,[78] oral cancer,[79] lung cancer,[80] or prostate cancer in men under 75.[81] Routine screening is not recommended for bladder cancer,[82] testicular cancer,[83] ovarian cancer,[84] pancreatic cancer,[85] or prostate cancer.[86]

The USPSTF recommends mammography for breast cancer screening every two years for those 50–74 years old; however, they do not recommend either breast self-examination or clinical breast examination.[87] A 2011 Cochrane review came to slightly different conclusions with respect to breast cancer screening stating that routine

mammography may do more harm than good.[88]

Japan screens for gastric cancer using photofluorography due to the high incidence there.[11]

Genetic testing

Gene	Cancer types
BRCA1, BRCA2	Breast, ovarian, pancreatic
HNPCC, MLH1, MSH2, MSH6, PMS1, PMS2	Colon, uterine, small bowel, stomach, urinary tract

Genetic testing for individuals at high-risk of certain cancers is recommended.[89] Carriers of these mutations may than undergo enhanced surveillance, chemoprevention, or preventative surgery to reduce their subsequent risk.[89]

Management

Many management options for cancer exist with the primary ones including: surgery, chemotherapy, radiation therapy, and palliative care. Which treatments are used depends upon the type, location and grade of the cancer as well as the person's health and wishes.

Surgery

Surgery is the primary method of treatment of most isolated solid cancers and may play a role in palliation and prolongation of survival. It is typically an important part of making the definitive diagnosis and staging the tumor as biopsies are usually required. In localized cancer surgery typically attempts to remove the entire mass along with, in certain cases, the lymph nodes in the area. For some types of cancer this is all that is needed for a good outcome.[90]

Chemotherapy

Chemotherapy in addition to surgery has proven useful in a number of different cancer types including: breast cancer, colorectal cancer, pancreatic cancer, osteogenic sarcoma, testicular cancer, ovarian cancer, and certain lung cancers.[90] The effectiveness of chemotherapy is often limited by toxicity to other tissues in the body.

Radiation

Radiation therapy involves the use of ionizing radiation in an attempt to either cure or improve the symptoms of cancer. It is used in about half of all cases and the radiation can be from either internal sources in the form of brachytherapy or external sources. Radiation is typically used in addition to surgery and or chemotherapy but for certain types of cancer such as early head and neck cancer may be used alone. For painful bone metastasis it has been found to be effective in about 70% of people.[91]

Alternative treatments

Complementary and alternative cancer treatments are a diverse group of health care systems, practices, and products that are not part of conventional medicine.[92] "Complementary medicine" refers to methods and substances used along with conventional medicine, while "alternative medicine" refers to compounds used instead of conventional medicine.[93] Most complementary and alternative medicines for cancer have not been rigorously studied or tested. Some alternative treatments have been investigated and shown to be ineffective but still continue to be marketed and promoted.[94]

Palliative care

Palliative care is an approach to symptom management that aims to reduce the physical, emotional, spiritual, and psycho-social distress experienced by people with cancer. Unlike treatment that is aimed at directly killing cancer cells, the primary goal of palliative care is to make the person feel better.

Palliative care is often confused with hospice and therefore only involved when people approach end of life. Like hospice care, palliative care attempts to help the person cope with the immediate needs and to increase the person's comfort. Unlike hospice care, palliative care does not require people to stop treatment aimed at prolonging their lives or curing the cancer.

Multiple national medical guidelines recommend early palliative care for people whose cancer has produced distressing symptoms (pain, shortness of breath, fatigue, nausea) or who need help coping with their illness. In people who have metastatic disease when first diagnosed, oncologists should consider a palliative care consult immediately. Additionally, an oncologist should consider a palliative care consult in any patient they feel has a prognosis of less than 12 months even if continuing aggressive treatment.[95][96][97]

Prognosis

Cancer has a reputation as a deadly disease. Taken as a whole, about half of people receiving treatment for invasive cancer (excluding carcinoma in situ and non-melanoma skin cancers) die from cancer or its treatment.[11] Survival is worse in the developing world.[11] However, the survival rates vary dramatically by type of cancer, with the range running from basically all people surviving to almost no one surviving.

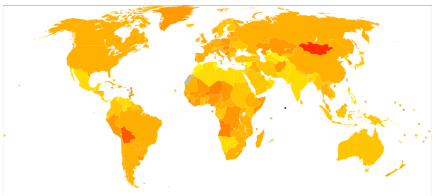
Those who survive cancer are at increased risk of developing a second primary cancer at about twice the rate of those never diagnosed with cancer.[98] The increased risk is believed to be primarily due to the same risk factors that produced the first cancer, partly due to the treatment for the first cancer, and potentially related to better compliance with screening.[98]

Predicting either short-term or long-term survival is difficult and depends on many factors. The most important factors are the particular kind of cancer and the patient's age and overall health. People who are frail with many other health problems have lower survival rates than otherwise healthy people. A centenarian is unlikely to survive for five years even if the treatment is successful. People who report a higher quality of life tend to survive longer.[99] People with lower quality of life may be affected by major depressive disorder and other complications from cancer treatment and/or disease progression that both impairs their quality of life and reduces their quantity of life. Additionally, patients with worse prognoses may be depressed or report a lower quality of life directly because they correctly perceive that their condition is likely to be fatal.

In 2007, the overall costs of cancer in the U.S. — including treatment and indirect mortality expenses (such as lost productivity in the workplace) — was estimated to be $226.8 billion. In 2009, 32% of Hispanics and 10% of children 17 years old or younger lacked health insurance; “uninsured patients and those from ethnic minorities are substantially more likely to be diagnosed with cancer at a later stage, when treatment can be more extensive and more costly.”[100]

Epidemiology

In 2008 approximately 12.7 million cancers were diagnosed (excluding non-melanoma skin cancers and other non-invasive cancers) and 7.6 million people died of cancer worldwide.[11] Cancers as a group account for approximately 13% of all deaths each year with the most common being: lung cancer (1.4 million deaths), stomach cancer (740,000 deaths), liver cancer (700,000 deaths), colorectal cancer (610,000 deaths), and breast cancer (460,000 deaths).[102] This makes invasive cancer the leading cause of death in the developed world and the second leading cause of death in the developing world.[11] Over half of cases occur in the developing world.[11]



Death rate from malignant cancer per 100,000 inhabitants in 2004. "WHO Disease and injury country estimates". World Health Organization. 2009. . Retrieved 11 November 2009.

Global cancer rates have been increasing primarily due to an aging population and lifestyle changes in the developing world.[11] The most significant risk factor for developing cancer is old age.[103] Although it is possible for cancer to strike at any age, most people who are diagnosed with invasive cancer are over the age of 65.[103] According to cancer researcher Robert A. Weinberg, "If we lived long enough, sooner or later we all would get cancer."[104] Some of the association between aging and cancer is attributed to immunosenescence,[105] errors accumulated in DNA over a lifetime,[106] and age-related changes in the endocrine system.[107]

Some slow-growing cancers are particularly common. Autopsy studies in Europe and Asia have shown that up to 36% of people have undiagnosed and apparently harmless thyroid cancer at the time of their deaths, and that 80% of men develop prostate cancer by age 80.[108][109] As these cancers did not cause the person's death, identifying them would have represented overdiagnosis rather than useful medical care.

The three most common childhood cancers are leukemia (34%), brain tumors (23%), and lymphomas (12%).[110] Rates of childhood cancer have increased by 0.6% per year between 1975 to 2002 in the United States[111] and by 1.1% per year between 1978 and 1997 in Europe.[110]

History

The earliest written record regarding cancer is from 3000 BC in the Egyptian Edwin Smith Papyrus and describes cancer of the breast.[112] Cancer however has existed for all of human history.[112] Hippocrates (ca. 460 BC – ca. 370 BC) described several kinds of cancer, referring to them with the Greek word *carcinos* (crab or crayfish).[112] This name comes from the appearance of the cut surface of a solid malignant tumour, with "the veins stretched on all sides as the animal the crab has its feet, whence it derives its name".[113] The Greek, Celsus (ca. 25 BC – 50 AD) translated *carcinos* into the Latin *cancer*, also meaning crab and recommended surgery as treatment.[112] Galen (2nd century AD) disagreed with the use of surgery and recommended purgatives instead.[112] These recommendations largely stood for 1000 years.[112]

Engraving with two views of a Dutch woman who had a tumor removed from her neck in 1689.

In the 15th, 16th and 17th centuries, it became more acceptable for doctors to dissect bodies to discover the cause of death.[114] The German professor Wilhelm Fabry believed that breast cancer was caused by a milk clot in a mammary duct. The Dutch professor Francois de la Boe Sylvius, a follower of Descartes, believed that all disease was the outcome of chemical processes, and that acidic lymph fluid was the cause of cancer. His contemporary Nicolaes Tulp believed that cancer was a poison that slowly spreads, and concluded that it was contagious.[115]

The physician John Hill described tobacco snuff as the cause of nose cancer in 1761.[114] This was followed by the report in 1775 by British surgeon Percivall Pott that cancer of the scrotum was a common disease among chimney sweeps.[116] With the widespread use of the microscope in the 18th century, it was discovered that the 'cancer poison' spread from the primary tumor through the lymph nodes to other sites ("metastasis"). This view of the disease was first formulated by the English surgeon Campbell De Morgan between 1871 and 1874.[117]

Society and culture

Though many diseases (such as heart failure) may have a worse prognosis than most cases of cancer, cancer is the subject of widespread fear and taboos. The euphemism, "after a long illness" is still commonly used (2012) reflecting an apparent stigma.[118] This deep belief that cancer is necessarily a difficult and usually deadly disease is reflected in the systems chosen by society to compile cancer statistics: the most common form of cancer—non-melanoma skin cancers, accounting for about one-third of all cancer cases worldwide, but very few deaths[119][120]—are excluded from cancer statistics specifically because they are easily treated and almost always cured, often in a single, short, outpatient procedure.[121]

Cancer is regarded as a disease that must be "fought" to end the "civil insurrection"; a War on Cancer has been declared. Military metaphors are particularly common in descriptions of cancer's human effects, and they emphasize both the parlous state of the affected individual's health and the need for the individual to take immediate, decisive actions himself, rather than to delay, to ignore, or to rely entirely on others caring for him. The military metaphors also help rationalize radical, destructive treatments.[122][123]

In the 1970s, a relatively popular alternative cancer treatment was a specialized form of talk therapy, based on the idea that cancer was caused by a bad attitude.[124] People with a "cancer personality"—depressed, repressed, self-loathing, and afraid to express their emotions—were believed to have manifested cancer through subconscious desire. Some psychotherapists said that treatment to change the patient's outlook on life would cure the cancer.[124] Among other effects, this belief allows society to blame the victim for having caused the cancer (by "wanting" it) or having prevented its cure (by not becoming a sufficiently happy, fearless, and loving person).[125] It also increases patients' anxiety, as they incorrectly believe that natural emotions of sadness, anger or fear shorten their lives.[125] The idea was excoriated by the notoriously outspoken Susan Sontag, who published *Illness as Metaphor* while recovering from treatment for breast cancer in 1978.[124] Although the original idea is now generally regarded as nonsense, the idea partly persists in a reduced form with a widespread, but incorrect, belief that deliberately cultivating a habit of positive thinking will increase survival.[125] This notion is particularly strong in breast cancer culture.[125]

Research

Because cancer is a class of diseases,[126][127] it is unlikely that there will ever be a single "cure for cancer" any more than there will be a single treatment for all infectious diseases.[128] Angiogenesis inhibitors were once thought to have potential as a "silver bullet" treatment applicable to many types of cancer, but this has not been the case in practice.[129]

Experimental cancer treatments are treatments that are being studied to see whether they work. Typically, these are studied in clinical trials to compare the proposed treatment to the best existing treatment. They may be entirely new treatments, or they may be treatments that have been used successfully in one type of cancer, and are now being tested to see whether they are effective in another type.[130] More and more, such treatments are being developed alongside companion diagnostic tests to target the right drugs to the right patients, based on their individual biology.[131]

Cancer research is the intense scientific effort to understand disease processes and discover possible therapies.

Research about cancer causes focuses on the following issues:

- Agents (e.g. viruses) and events (e.g. mutations) which cause or facilitate genetic changes in cells destined to become cancer.
- The precise nature of the genetic damage, and the genes which are affected by it.
- The consequences of those genetic changes on the biology of the cell, both in generating the defining properties of a cancer cell, and in facilitating additional genetic events which lead to further progression of the cancer.

The improved understanding of molecular biology and cellular biology due to cancer research has led to a number of new, effective treatments for cancer since President Nixon declared "War on Cancer" in 1971. Since 1971 the United States has invested over $200 billion on cancer research; that total includes money invested by public and private sectors and foundations.[132] Despite this substantial investment, the country has seen a five percent decrease in the cancer death rate (adjusting for size and age of the population) between 1950 and 2005.[133]

In pregnancy

Because cancer is largely a disease of older adults, it is not common in pregnant women. Cancer affects approximately 1 in 1,000 pregnant women.[134] The most common cancers found during pregnancy are the same as the most common cancers found in non-pregnant women during childbearing ages: breast cancer, cervical cancer, leukemia, lymphoma, melanoma, ovarian cancer, and colorectal cancer.[134]

Diagnosing a new cancer in a pregnant woman is difficult, in part because any symptoms are commonly assumed to be a normal discomfort associated with pregnancy.[134] As a result, cancer is typically discovered at a somewhat later stage than average in many pregnant or recently pregnant women. Some imaging procedures, such as MRIs (magnetic resonance imaging), CT scans, ultrasounds, and mammograms with fetal shielding are considered safe during pregnancy; some others, such as PET scans are not.[134]

Treatment is generally the same as for non-pregnant women.[134] However, radiation and radioactive drugs are normally avoided during pregnancy, especially if the fetal dose might exceed 100 cGy. In some cases, some or all treatments are postponed until after birth if the cancer is diagnosed late in the pregnancy. Early deliveries to speed the start of treatment are not uncommon. Surgery is generally safe, but pelvic surgeries during the first trimester may cause miscarriage. Some treatments, especially certain chemotherapy drugs given during the first trimester, increase the risk of birth defects and pregnancy loss (spontaneous abortions and stillbirths).[134]

Elective abortions are not required and, for the most common forms and stages of cancer, do not improve the likelihood of the mother surviving or being cured.[134] In a few instances, such as advanced uterine cancer, the pregnancy cannot be continued, and in others, such as an acute leukemia discovered early in pregnancy, the pregnant woman may choose to have abortion so that she can begin aggressive chemotherapy without worrying about birth defects.[134]

Some treatments may interfere with the mother's ability to give birth vaginally or to breastfeed her baby.[134] Cervical cancer may require birth by Caesarean section. Radiation to the breast reduces the ability of that breast to produce milk and increases the risk of mastitis. Also, when chemotherapy is being given after birth, many of the drugs pass through breast milk to the baby, which could harm the baby.[134]

Notes

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[2] http://apps.who.int/classifications/icd10/browse/2010/en#/C97

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[4] http://www.icd9data.com/getICD9Code.ashx?icd9=239

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