REVIEW ON CANCER AND TUMOR DISEASES

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ABSTRACT

Tumor is a disease that involves abnormal growth with the potential to invade or spread to other parts of the body. Not all tumors are cancerous; tumors do not spread to other parts of the body. Possible signs and symptoms include: a new lump, abnormal bleeding, a prolonged cough, unexplained weight loss, and a change in bowel movements among others. While these symptoms may indicate cancer, they may also occur due to other issues. There are over 100 different known cancers that affect humans.

KEYWORDS: Million, Human, Common, Change

INTRODUCTION

In 2012 about more than 14 million new cases of cancer occurred globally (not including skin cancer other than melanoma).[1] It caused about 8.2 million deaths or 14.6% of all human deaths.[2-6] The most common types of cancer in males are lung cancer, prostate cancer, colorectal cancer, and stomach cancer, and in females, the most common types are breast cancer, colorectal cancer, lung cancer, and cervical cancer.[7-9] If skin cancer other than melanoma were included in total new cancers each year it would account for around 40% of cases.[10-18] In children, acute lymphoblastic leukemia and brain tumors are most common except in Africa where non-Hodgkin lymphoma occurs more often.[14] In 2012, about 165,000 children under 15 years of age were diagnosed with cancer. The risk of cancer increases significantly with age and many cancers occur more commonly in developed countries.[6] Rates are increasing as more people live to an old age and as lifestyle changes occur in the developing world.[19] The financial costs of cancer have been estimated at $1.16 trillion US dollars per year as of 2010.[20]

Cancers are a large family of diseases that involve abnormal cell growth with the potential to invade or spread to other parts of the body.¹²³ They form a subset of neoplasm. A neoplasm or tumor is a group of cells that have undergone unregulated growth, and will often form a mass or lump, but may be distributed diffusely.¹²¹²²

Six Characteristics of Cancer Have Been Proposed

- Self-sufficiency in growth signaling
- Insensitivity to anti-growth signals
- Evasion of apoptosis
- Enabling of a limitless replicative potential
- Induction and sustainment of angiogenesis
• Activation of metastasis and invasion of tissue.\textsuperscript{[13]}

The progression from normal cells to cells that can form a discernible mass to outright cancer involves multiple steps known as malignant progression.

![Figure 1](image1.png)  
**Figure 1**  

![Figure 2](image2.png)  
**Figure 2**  

**Diagnosis Cancer by Ray and MRI Technique**

MRI is very good at finding and pinpointing some cancers. An MRI with contrast dye is the best way to see brain tumors. Using MRI, doctors can sometimes tell if a tumor is benign (not cancer) or malignant (cancer).

MRI can also be used to look for signs that cancer may have metastasized (spread) from where it started to another part of the body.

MRI images can also help doctors plan treatment such as surgery or radiation therapy.

Special MRI machines, now available in some hospitals, are designed just for looking inside the breast. This is called an MRI with dedicated breast coils. Breast MRI is recommended along with mammograms to look for breast cancer in women at high risk for breast cancer. At this time MRI is not used by itself to detect breast cancer early. (To learn more about this, see Breast Cancer: Early Detection.) Breast MRI can also be used in women who have already been diagnosed with breast cancer to better determine the actual size of the cancer and to look for any other cancers in the breast.
An MRI scanner is a cylinder or tube that holds a large, very strong magnet. As you lie on a table that slides within the tube, the device surrounds you with a powerful magnetic field. The magnetic force causes the nuclei (centers) of hydrogen atoms in your body to line up in one direction. Once the atoms are lined up, the MRI machine gives off a burst of radiofrequency waves. These waves cause the hydrogen nuclei to change direction. When they return to their original position, they give off certain signals that the scanner detects. Hydrogen nuclei in the body tissues change direction in different ways. A computer takes the signals from these changes and converts them into a black and white picture.

Contrast materials can be put into the body through a vein to improve the quality of the image. Once absorbed by the body, these agents speed up the rate at which tissue responds to the magnetic and radio waves. As a result, the signals produce stronger, clearer pictures.

**Figure 3**

### Preparing for the Test

When you schedule your MRI, you will get detailed instructions about how to prepare. You may need to avoid eating for two or more hours before the test, but usually you will not need to make any special preparations.

Tell your doctor about all medications you are taking, as well as any drug allergies or any other medical conditions you may have. Women should tell their doctors if there is any chance that they may be pregnant. In addition, it is important to tell your doctor and the technologist performing the MRI about any metal implants or metal fragments you have in your body. These can cause serious, and even fatal, complications when exposed to the strong magnetic pull generated by the MRI. People with pacemakers, for example, cannot have an MRI.

Before your appointment, you may want to check with your insurance provider to find out whether the cost of the MRI will be covered and if there are any additional costs you may need to pay yourself. Once you arrive for your scan, you will be asked to sign a consent form that states you understand the benefits and risks of the MRI and agree to have the test done. Talk with your doctor about any concerns you have about the MRI. Also, consider asking whether you can bring music with you to the scan; some facilities allow patients to listen to music through headphones during their MRI.

### During the Test

When you arrive for your MRI, you will need to remove any jewelry or other metal objects you are wearing. You may also need to change into a hospital gown.
Depending on the part of your body that will be scanned, you may be given a contrast medium (a special dye) through an intravenous (IV) line or orally (by mouth). If the dye is given through an IV, a nurse or doctor will insert a small needle into a vein in your arm or hand, and a saline solution (a mixture of salt and water) will flow through the line until the dye is injected at a specific point during the test. The dye will travel through the bloodstream and help create a clearer picture of specific parts of your body.

A technologist will help position you on a moveable exam table outside of the MRI machine. You will lie on your back with your arms at your side and your head on a headrest. A “coil” will be positioned over or around the part of your body that will be studied to create a clear picture of that area.

When you are in the correct position, the exam table will slide through the hole in the center of the MRI machine, which looks like a large donut. The standard MRI machine has a narrow, tunnel-like opening. Some facilities have less confining or “open” MRI machines.

You will need to lie still as the machine takes a series of pictures. Each series will take up to 15 minutes, and you may need to have two to six series before the test is over. An MRI will usually last up to 90 minutes. The technologist should be able to give you a time estimate before you begin.

During the scan, the technologist will be in a nearby computer room, separated by a window. The technologist will be able to see you, and you will be able to communicate at all times through an intercom system. The part of your body that is being examined may feel warm during the MRI; this is normal.

You will know when the machine is taking pictures because you will hear loud tapping or knocking sounds. Once the MRI is complete, you may be asked to stay on the exam table while a radiologist reviews the pictures to see if more are needed.

An MRI is not painful. However, if you receive an IV, you may feel discomfort when the needle is inserted, and the saline solution in the IV may cause a cool feeling at the injection site. In addition, you will need to lie still for most of the scan, which could become uncomfortable. The loud sounds coming from the machine may also make you uncomfortable, and you may be given earplugs to wear during the scan. If you are claustrophobic (afraid of small spaces), tell the technologist before beginning the examination. The radiologist may be able to give you a medication to help you relax (sedative).

Breast MRI for Diagnosis and Monitoring

The value of breast MRI for breast cancer detection remains uncertain. Some doctors believe MRI can distinguish a breast cancer from normal breast gland tissue better than other techniques. But breast MRI is expensive and requires highly specialized equipment and highly trained experts. Relatively few breast MRI centers exist, especially outside of major cities. And even at its best, MRI produces many uncertain findings. Some radiologists call these “unidentified bright objects,” or UBOs. MRI also cannot detect calcifications (calcium deposits in breast tissue that could be a sign of cancer). Finally, MRI can dislodge certain metal devices, such as pacemakers, in some people.

In some situations, however, breast MRI can be useful in gathering more information about an area in the breast that is suspicious or already confirmed to be cancerous. Possible uses include:
• Evaluating a person who has a palpable mass (a mass that can be felt) that isn’t visible with ultrasound or mammography

• Evaluating a lesion in the densely glandular breast of a young woman. Young women tend to have dense breast tissue, which makes it difficult to see abnormal areas on imaging studies.

• Evaluating a person who has breast cancer cells in an underarm lymph node, but no breast mass that doctors are able to feel or to see on a mammogram. In these cases, where mastectomy is typically recommended, MRI can help find the precise site of the cancer’s origin within the breast. Finding the cancer’s site of origin can expand a woman’s treatment options from only mastectomy to include lumpectomy plus radiation.

• Determining if a cancer is limited to one area of the breast, or if it is “multicentric” and involves more than one area. Knowing this affects treatment choices, since mastectomy is necessary for multicentric disease. MRI can be particularly useful for women with invasive lobular cancer, which has a tendency to be diffuse or multicentric.

• Checking a woman’s other breast for signs of cancer after she receives her initial cancer diagnosis. The American Cancer Society recommends that breast MRI be used to check the other breast for any signs of cancer.

• Examining breast tissue in women who have had silicone breast implants. MRI scanning can detect leakage from a silicone-filled breast implant, since it easily distinguishes silicone gel from surrounding normal breast and chest wall tissues.

After treatment for breast cancer, MRI can be useful for checking scar tissue in women who have undergone lumpectomy. Any significant changes could suggest a return of the breast cancer.

Finally, MRI scans of other parts of the body such as the brain, spinal cord, or bones may be useful in people who are known or suspected to have metastatic breast cancer (cancer that has traveled outside the breast to other areas of the body). For example, a person who has progressive back pain, or who develops new weakness or numbness in the arms or legs (not just hands or feet), can have an MRI scan of her back. The scan can help identify serious conditions such as the possible presence of a spinal tumor or brain metastasis.

Causes of Cancer

The causes are due to environmental factors. The remaining 5–10% are due to inherited genetics.[5] Environmental, as used by cancer researchers, means any cause that is not inherited genetically, such as lifestyle, economic and behavioral factors, and not merely pollution.[17] 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.[5]

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. Excepting the rare transmissions that occur with pregnancies and only a marginal few organ donors, cancer is generally not a transmissible disease.[18]
Chemicals

*Via Alcohol and cancer and Smoking and cancer*

The incidence of lung cancer is highly correlated with smoking.

Exposure to particular substances have been linked to specific types of cancer. These substances are called *carcinogens*. Tobacco smoking, for example, causes 90% of lung cancer.[19] It also causes cancer in the larynx, head, neck, stomach, bladder, kidney, esophagus and pancreas.[3] Tobacco smoke contains over fifty known carcinogens, including nitrosamines and polycyclic aromatic hydrocarbons.[11]

Tobacco is responsible for about one in three of all cancer deaths in the developed world,[12] and about one in five worldwide.[11] 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.[13]

In Western Europe, 10% of cancers in males and 3% of all cancers in females are attributed to alcohol exposure, especially cancer of the liver and of the digestive tract.[15] Cancer related to substance exposures at work is believed to represent between 2–20% of all cases.[16] Every year, at least 200,000 people die worldwide from cancer related to their workplaces.[17] Millions of workers run the risk of developing cancers such as lung cancer and mesothelioma from inhaling tobacco smoke or asbestos fibers on the job, or leukemia from exposure to benzene at their workplaces.[17]

Infection

Worldwide approximately 18% of cancer deaths are related to infectious diseases.[25] This proportion varies in different regions of the world from a high of 25% in Africa to less than 10% in the developed world.[5] Viruses are the usual infectious agents that cause cancer but cancer bacteria and parasites may also have an effect.

A virus that can cause cancer is called an *oncogenic virus*. These include human papilloma virus (cervical carcinoma), Epstein–Barr virus (B-cell lympho proliferative disease and nasopharyngeal carcinoma), Kaposi's sarcoma herpes virus (Kaposi's sarcoma and primary effusion lymphomas), hepatitis B and hepatitis C viruses (hepatocellular carcinoma), and human T-cell leukemia virus-1 (T-cell leukemia). Bacterial infection may also increase the risk of cancer, as seen in *Helicobacter pylori*-induced gastric carcinoma.[13] 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).[14]

Radiation

Up to 10% of invasive cancers are related to radiation exposure, including both ionizing radiation and non-ionizing ultraviolet radiation.[5] Additionally, the vast majority of non-invasive cancers are non-melanoma skin cancers caused by non-ionizing ultraviolet radiation, mostly from sunlight. Sources of ionizing radiation include medical imaging and radon gas.

Ionizing radiation is not a particularly strong mutagen.[15] Residential exposure to radon gas, for example, has similar cancer risks as passive smoking.[5] 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.[4] Radiation can cause cancer in most parts of the
body, in all animals, and at any age. Children and adolescents are twice as likely to develop radiation-induced leukemia as adults; radiation exposure before birth has ten times the effect.\textsuperscript{24}

Medical use of ionizing radiation is a small but 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.\textsuperscript{15} It is also used in some kinds of medical imaging.\textsuperscript{16}

Prolonged exposure to ultraviolet radiation from the sun can lead to melanoma and other skin malignancies.\textsuperscript{17} 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.\textsuperscript{17}

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.\textsuperscript{18} However, studies have not found a consistent link between cell phone radiation and cancer risk.\textsuperscript{19}

**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 that has a large effect on cancer risk and these cause less than 3–10% of all cancer.\textsuperscript{5} Some of these syndromes include: certain inherited mutations in the genes \textit{BRCA1} and \textit{BRCA2} with a more than 75% risk of breast cancer and ovarian cancer,\textsuperscript{25} and hereditary nonpolyposis colorectal cancer (HNPCC or Lynch syndrome), which is present in about 3% of people with colorectal cancer,\textsuperscript{11} among others.

**Physical Agents**

Some substances cause cancer primarily through their physical, rather than chemical, effects on cells.\textsuperscript{12} A prominent example of this is prolonged exposure to asbestos, naturally occurring mineral fibers that are a major cause of mesothelioma, which is a cancer of the serous membrane, usually the serous membrane surrounding the lungs.\textsuperscript{25} 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.\textsuperscript{12} Non-fibrous particulate materials that cause cancer include powdered metallic cobalt and nickel, and crystalline silica (quartz, cristobalite, and tridymite).\textsuperscript{5} Usually, physical carcinogens must get inside the body (such as through inhaling tiny pieces) and require years of exposure to develop cancer.\textsuperscript{12}

Physical trauma resulting in cancer is relatively rare.\textsuperscript{3} Claims that breaking bones resulted in bone cancer, for example, have never been proven.\textsuperscript{3} Similarly, physical trauma is not accepted as a cause for cervical cancer, breast cancer, or brain cancer.\textsuperscript{3} 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.\textsuperscript{13} Frequently drinking scalding hot tea may produce esophageal cancer.\textsuperscript{5} 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.\textsuperscript{13} However, repeated injuries to the same tissues might promote excessive cell proliferation, which could then increase the odds of a cancerous mutation.
It is controversial whether chronic inflammation can directly cause mutation.\[^{13, 24}\] It is recognized, however, that inflammation can contribute to proliferation, survival, angiogenesis and migration of cancer cells by influencing the microenvironment around tumors.\[^{1, 28, 16}\] Furthermore, oncogenes are known to build up an inflammatory pro-tumorigenic microenvironment.\[^{7}\]

**Hormones**

Some hormones play a role in the development of cancer by promoting cell proliferation.\[^{8}\] Insulin-like growth factors and their binding proteins play a key role in cancer cell proliferation, differentiation and apoptosis, suggesting possible involvement in carcinogenesis.\[^{9}\]

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.\[^{1, 8}\] 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.\[^{8}\] 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.\[^{5}\] Men of Asian ancestry, with the lowest levels of testosterone-activating androstanediol glucuronide, have the lowest levels of prostate cancer.\[^{5}\]

Other factors are also relevant: obese people have higher levels of some hormones associated with cancer and a higher rate of those cancers.\[^{5}\] Women who take hormone replacement therapy have a higher risk of developing cancers associated with those hormones.\[^{5, 8}\] On the other hand, people who exercise far more than average have lower levels of these hormones, and lower risk of cancer.\[^{18}\] Osteosarcoma may be promoted by growth hormones.\[^{5}\] Some treatments and prevention approaches leverage this cause by artificially reducing hormone levels, and thus discouraging hormone-sensitive cancers.\[^{8}\]

**Pathophysiology**

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

**Genetics**

Cancer is fundamentally a disease of tissue growth regulation failure. In order for a normal cell to transform into a cancer cell, the genes that regulate cell growth and differentiation must be altered.\[^{6}\]

The affected genes are divided into two broad categories. Oncogenes are genes that promote cell growth and reproduction. Tumor suppressor genes are genes that 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.\[^{6}\]

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, leading to 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.\(^ {\text{[2]}}\)

The Errors that 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 tumor 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.\(^ {\text{[3]}\)} Clonal evolution leads to intra-tumour heterogeneity that complicates designing effective treatment strategies.

Characteristic abilities developed by cancers are divided into a number of categories. Six categories were originally proposed, in a 2000 article called "The Hallmarks of Cancer" by Douglas Hanahan and Robert Weinberg: evasion of apoptosis, self-sufficiency in growth signals, insensitivity to anti-growth signals, sustained angiogenesis, limitless replicative potential, and metastasis. Based on further work, the same authors added two more categories in 2011: reprogramming of energy metabolism and evasion of immune destruction.\(^ {\text{[3][4]}}\)
Epigenetics

The central role of DNA damage and epigenetic defects in DNA repair genes in carcinogenesis.

Classically, cancer has been viewed as a set of diseases that are driven by progressive genetic abnormalities that include mutations in tumor-suppressor genes and oncogenes, and chromosomal abnormalities. However, it has become apparent that cancer is also driven by epigenetic alterations.

Epigenetic alterations refer to functionally relevant modifications to the genome that do not involve a change in the nucleotide sequence. Examples of such modifications are changes in DNA methylation (hypermethylation and hypomethylation) and histone modification and changes in chromosomal architecture (caused by inappropriate expression of proteins such as HMGA2 or HMGA1). Each of these epigenetic alterations serves to regulate gene expression without altering the underlying DNA sequence. These changes may remain through cell divisions, last for multiple generations, and can be considered to be epimutations (equivalent to mutations).

Epigenetic alterations occur frequently in cancers. As an example, Schnekenburger and Diederich listed protein coding genes that were frequently altered in their methylation in association with colon cancer. These included 147 hypermethylated and 27 hypomethylated genes. Of the hypermethylated genes, 10 were hypermethylated in 100% of colon cancers, and many others were hypermethylated in more than 50% of colon cancers.

While large numbers of epigenetic alterations are found in cancers, the epigenetic alterations in DNA repair genes, causing reduced expression of DNA repair proteins, may be of particular importance. Such alterations are thought to occur early in progression to cancer and to be a likely cause of the genetic instability characteristic of cancers.

Reduced expression of DNA repair genes causes deficient DNA repair. This is shown in the figure at the 4th level from the top. (In the figure, red wording indicates the central role of DNA damage and defects in DNA repair in progression to cancer.) When DNA repair is deficient DNA damages remain in cells at a higher than usual level (5th level from the top in figure), and these excess damages cause increased frequencies of mutation and/or epimutation (6th level from top of figure). Mutation rates increase substantially in cells defective in DNA mismatch repair or in homologous recombinational repair (HRR). Chromosomal rearrangements and aneuploidy also increase in HRR defective cells.

Higher levels of DNA damage not only cause increased mutation (right side of figure), but also cause increased epimutation. During repair of DNA double strand breaks, or repair of other DNA damages, incompletely cleared sites of repair can cause epigenetic gene silencing.

Deficient expression of DNA repair proteins due to an inherited mutation can cause an increased risk of cancer. Individuals with an inherited impairment in any of 34 DNA repair genes (see article DNA repair-deficiency disorder) have an increased risk of cancer, with some defects causing up to a 100% lifetime chance of cancer (mutations). Germ line DNA repair mutations are noted in a box on the left side of the figure, with an arrow indicating their contribution to DNA repair deficiency. However, such germline mutations (which cause highly penetrant cancer syndromes) are the cause of only about 1 percent of cancers.

In sporadic cancers, deficiencies in DNA repair are occasionally caused by a mutation in a DNA repair gene, but are much more frequently caused by epigenetic alterations that reduce or silence expression of DNA repair genes. This is indicated in the figure at the 3rd level from the top. Many studies of heavy metal-induced carcinogenesis show that such...
heavy metals cause reduction in expression of DNA repair enzymes, some through epigenetic mechanisms. In some cases, DNA repair inhibition is proposed to be a predominant mechanism in heavy metal-induced carcinogenicity. In addition, there are frequent epigenetic alterations of the DNA sequences coding for small RNAs called microRNAs (or miRNAs). MiRNAs do not code for proteins, but can “target” protein-coding genes and reduce their expression.

Cancers usually arise from an assemblage of mutations and epimutations that confer a selective advantage leading to clonal expansion (see Field defects in progression to cancer). Mutations, however, may not be as frequent in cancers as epigenetic alterations. An average cancer of the breast or colon can have about 60 to 70 protein-altering mutations, of which about three or four may be “driver” mutations, and the remaining ones may be “passenger” mutations. As pointed out above under genetic alterations, cancer is caused by failure to regulate tissue growth, when the genes that regulate cell growth and differentiation are altered. It has become clear that these alterations are caused by both DNA sequence mutation in oncogenes and tumor suppressor genes as well as by epigenetic alterations. The epigenetic deficiencies in expression of DNA repair genes, in particular, likely cause an increased frequency of mutations, some of which then occur in oncogenes and tumor suppressor genes.

Metastasis

Metastasis is the spread of cancer to other locations in the body. The new tumors are called metastatic tumors, while the original is called the primary tumor. Almost all cancers can metastasize. Most cancer deaths are due to cancer that has spread from its primary site to other organs (metastasized).

Metastasis is very common in the late stages of cancer, and it can occur via the blood or the lymphatic system or both. The typical steps in metastasis are local invasion, intravasation into the blood or lymph, circulation through the body, extra vasation into the new tissue, proliferation, and angiogenesis. Different types of cancers tend to metastasize to particular organs, but overall the most common places for metastases to occur are the lungs, liver, brain, and the bones.

Types of Cancer

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 develops 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%.

- **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 aleiomyoma (the common name of this frequently occurring benign tumor in the uterus is fibroid). Confusingly, some types of cancer use the –noma 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.

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