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Cancer and Neoplasia Factsheet

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CANCER AND NEOPLASIA

Juraj Artner, July 28, 2001

Introduction

"More than 1,500 people will die of cancer today, according to data from the American Cancer Society." (1)
The Digital Collegian
"Each year cancer is newly diagnosed in 9 million people worldwide and it causes 5 million deaths. It is second to cardiovascular disease as a cause of death in developed countries, and overall causes 10% of all deaths in the world." (2)
WHO
"While deaths from heart disease and stroke have declined, cancer deaths have remained relatively constant since 1950, at about 125 deaths per 100,000 people." (3)
Ameristat

1. What is Cancer

The term "cancer" is used synonymous with the term malignant neoplasia and describes a disease, that is characterised by uncontrolled, abnormal growth of cells (proliferation). The first historical description of this condition was in relation to breast carcinoma (Hippocrates), but malignant cancer masses, also called malignant tumours (lat.:mass), have been found in Egyptian mummies, about 5000 years old. They are described in ancient medical writings, such as the Edwin Smith and Ebers papyrusses, both written about 3,500 years ago. (4) Using the greek term "karkinos", which means cancer, Hippocrates (460-377 b.Chr.) described the visual appearance of the cellular mass, which looks like the animal with its eminences. (5) The latin translation of "karkinos" is "cancer", first used by Galen (199 a.Chr.). (6, 7) The term "neoplasia" describes a new tissue or cell growth, mostly from the own-body-cells (exception: Choriocarcinoma, which developes from embryonal-placentar tissue). A neoplasia can be benign or malignant:

1.1. Benign Neoplasia
The prefix "benign" means that in most cases the neoplasia does not grow agressive into the normal tissue, it does not destroy it, it grows slowly, does not spread in further areas of the body, it has a better differenciation, a fibrous capsule (see the image Nr.1) and has a good prognosis. This does not mean, that a benign neoplasia cannot become a serious problem. Depending on the localisation, a neoplasia can compress structures in the brain and damage them, it can obturate a duct (and damage for example the biliar secretion). But in most cases, like already mentioned, it does not impact the life expectancy of the patient. Examples: Breast Adenoma, Enteral Polyp.

1.2. Malignant Neoplasia
The prefix "malignant" describes a fast growing tumour, consisting of anaplastic cells (lack of differentiation), invading and destroying the tissue and spreading in further areas of the body (see the image Nr.1). This spreading is called metastasis. Most malignant neoplasms reduce the life expectancy of the patient. (8) Examples: Breast Adenocarcinoma, Colonorectal Carcinoma, Haemagiosarcoma.

For more information about benign and malignant neoplasia, like the nomenclature, grading, etc...read the chapter 6. Nomenclature.

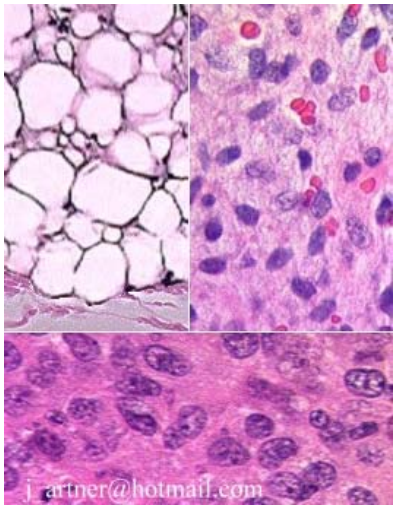
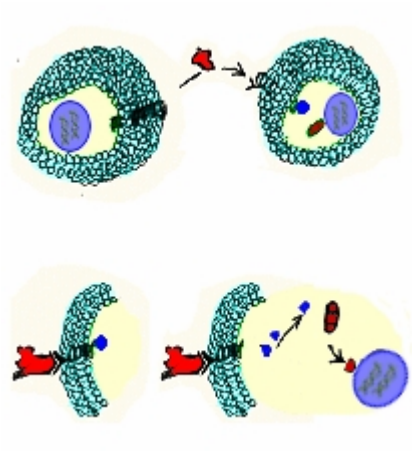


Image Nr.1 - Benign vs. Malignant Neoplasia
The superior part of the image shows fat- tissue, on the left benign- (Lipoma), on the right malignant (Liposarcoma) transformed. The benign Lipoma has large cells and is well differentiated. The cellular structures are typical for the tissue of origin. See also the capsule at the bottom of the Lipoma as a sign of non-invading benign neoplasm. The right upper part (malignant Liposarcoma) shows a lack of differentiation. The cellular structure does not imitate the tissue of origin, there is also no capsule. The cells are smaller than normal fat- cells, with a variable cell shape. See also the hyperchromatic (good colored/ high affinity to histologic color) nuclei, because of the increased genetic material (higher growth activity).
The inferior part of the image shows a complete anaplastic tissue of a carcinoma, the tissue of origin cannot be determined. See the variable cellular and nunclear size and shape. See also the nuclear-cytoplasmatic ratio and the hyperchromatic nuclei, representing the increased mitotic (growth) activity.

2. Cancerogenesis and malignant Transformation
Both terms describe the process in which a cell or a cell- clone becomes malignant neoplasia (cancer). The transformation beginns by a cellular damage, to be more specific, by a damage on the genetic material of the cell. The damage can be caused by chemicals, physical agents, virus or bacterial infection, the so called carcinogenic agents (see chapter 2.1.5) . This process is at the beginning of a malignant transformation and is called initiation:



2.1. Initiation

Most human cells have a core, with the genetic information in. This genes affect all cellular procedures,like the growth, the morphology, specification and even the cell death. The genetic material is something like a software for the living organism. It is important for the further understanding of the cancerogenesis process to explain some structures redarding the cellular biology and genetics:
A tissue cell stands never alone, it always communicates with its environment. It gets and sends molecular signs (signal) through the cell membrane. This molecular signs find the specific structure on the outer cell membrane of the other cell, which is called receptor. The receptor and the molecular signal fit into each other like a key and a keyhole. After the chemical bond of these two structures the signal is forwarded into the cell. This forwarding, called signal transduction is provided by specific molecular structures, called second messengers. (9) These second messengers provide a signal cascade, enhance and forward the signal through the cell (see the image Nr.2). The final targets of this messengers are membrane channels, enzymes, transcription factors, core proteins, mechanic structures like proteins which stabilize the cell membrane or move the cell with specific eminencies,... The fact, that this structures also provide the switch- off of the signal- cascade is also very important.

Image Nr.2 - Simple Signal Transduction
The superior part of the image shows the molecular signal between two cells (red). The left cell is the secretor, right the acceptor with the specific receptor on the outer membrane combined with a second messenger on the inner membrane (blue). The left inferior part shows the chemical bond between signal and receptor, the right inferior part shows the signal forwarding (transduction) into the inner part of the cell - the second messenger (blue) activates/ deactivates an enzyme (dark red). This image is simpified. In the reality, the second messenger activates more enzymes, what mean an enhancement of the signal- quantity.

2.1.1. Proto- Oncogenes

Like already mentioned, also transcription factors can be activated/ deactivated by this mechanism, so that the controlled/ uncontrolled cell growth is also under the influence of such a process. An alteration of such a structure like the second messenger can cause a cell-deregulation. The part of the human genome, which encodes such a cell- regulating- structure, is called proto- oncogen, that means it can be involved in cancer initiation. Example: The specific part of the genetic code, which encodes a growth factor receptor is damaged by radiation. Our proto- oncogen changed into an oncogen. The result is, that a modified receptor gets produced by the cell. This receptor has in our example a damaged switch- off mechanism, so that the cell has to face an endless growth stimulation and the result is an unconrolled growth.
The cellular proto- oncogene- groups are:
I. Growth Factors (cell to cell stimulation- signals)
II. Growth Factor Receptors (stimulation- signal- receptors)
III. Signal Transduction Proteins (second messenger,...)
IV. Nuclear Regulatory Factors (genetic material- transcription- factors) (10)
V. Cyclins (cell- cycle regulation factors) (11)

An oncogene can be activated by a point mutation, which occurs when a small segment of the gene is altered by a carcinogen (see chapter 2.1.5. carcinogens). It can also be activated by chromosomal breaks, translocations and deletions, when an proto- oncogene gets placed near a regulatory genome sequence which activates it.

Another way an oncogene can be activated is through amplification, when a proto- oncogene is replicated many times in a cell. The cell produces more oncogene encoded structures.

2.1.2. Cancer Supressor Genes
They controll the cellular proliferation by inhibiting the cell growth. An alteration of this structures must be on both chromosomes (alleles), to initiate a malignant transformation. Example: A total lack of the cancer supressor gene RB1 causes Retinoblastoma, a malignant eye cancer of the childhood.(12)

2.1.3. Genome Repair
This is a very important mechanism, which repairs the human genetic material after a damage. It consists of enzymes like Endonuclease, which can detach a damaged part of the genetic code, DNA-ligase, which makes the final bond between a repaired and the normal genetic material. Example: Xeroderma pigmentosum is a disease with an inherited damage of genome repair mechanism. The patients are sensitive to light (UV), sometimes they have a neural damage, and the incidence of skin cancer is increased. (13) The reason for this higher incidence is the following: The ultraviolett part of the sunlight often causes genetic damages like Thymin-dimers. An other part of the sunlight activates in normal tissue the genome repair mechanisms, a reason why people should prefer the natural sunlight and not a solarium which does not have this light fraction. Patients with Xeroderma pigmentosum have a damage of the repair mechanism, so there is nothing to be activated and the genetic material has to face the whole physical damage, caused by the uv-light part. In such a case, an alteration of a proto- oncogene or a supressor gene will result in a consecutive malignant transformation.

2.1.4. Apoptosis Regulators
Apoptosis means a controlled cellular death, something like a cellular suicide. A cell has its specific life expectancy, depending on the tissue and the differentiation. After a limited time period, a cell produces suicid proteins, which destroy the genetic material, the membranes and other cellular structures by a self- digestion. Such a cell becomes smaller in size and the genome decreases. This apoptosis mechanism is also controlled by genes. These genes are natural inhibitors of an uncontrolled cell proliferation. A damage of this mechanism is often seen in leukaemia, where a white bood cell clone expands and does not (want) die.

2.1.5. Carcinogenic Agents
Carcinogenic Agents, also called Carcinogens, are causing genetic damage and so initiating a malignant transformation. There are four groups of Carcinogenes, they all have in common, that they damage the genome, the difference between them is only the way, how they damage it:
chemicals
physical agents
virus
bacterial infections

I. Chemical Carcinogens
are molecular structures which can interact with the normal human genome in a chemical reaction, f.e. by a chemical bond, and induce cancer. There are direct acting chemical carcinogens or indirect acting, what means that some chemicals can become carcinogenes by the metabolic conversion in the body (f.e.: by the P450 liver oxygenase system, called bioactivation) and some chemicals are carcinogenes already before they get into the body. Cancer induction by chemical substancies was already described in the year 1775, by Percival Pott. This English physician observed that the high incidence of scrotal cancer in chimney sweeps was due to their exposure to coal tars. (14) This factsheet would explode, if I would try to list all carcinogens or suspected carcinogens, so I can list only few examples (interrested readers can visit the reference pages (15, 16) for a comprehensive list of carcinogens):

Polycyclic aromatic hydrocarbons - can be found in tar (coal, tobacco products), can induce scrotal or lung cancer,
Aromatic amines - are used in the production of dye for food coloring, can induce bladder carcinoma,
Aflatoxin - found in some fungi, can induce hepatocellular (liver) cancer,
Arsenic - can induce skin cancer,
Asbestos - used f.e. in old buildings, can induce mesothelioma (lung capsule cancer) or lung cancer

II. Physical Carcinogens
are the different types of radiation, like UV (Ultra Violet) and the ionizing radiation (x-ray, atomic energy dissasters radiation). The damage is set on the genome, similar to chemical carcinogens: UV radiation induces the building of thymine- dimers in the human genome, what can lead to skin cancer, like melanoma. The cellular genome rapair mechanism play an important role in this process (see also chapter 2.1.3. genome repair). The reason, why most people dont get skin cancer during vacation in sunny places is the following: The normal sunlight with the damaging UV-component has also special spectral components, which activate the normal cellular repair mechanisms. This spectral components are not included in solarium, where only the UV-spectral component is active. This means, that the body has to face only the damaging component without or with a lower activated protective component.
Ionizing radiation can be divided into particulate (alpha, beta) and non-particulate (electromagnetic- gamma) radiation. Ionization means, that the atom capsule is changed, f.e. by a loss of an electrone. Such a change means also a change in the chemical behavior of the atom or molecule. Two mechanisms impact the genetic and cellular material: First, the radiation directly ionizes cellular molecules (direct ionization). Second, an interaction with cellular water and oxygen leads to free radical production, which damage the genome and other cellular structures. A radical is an atom with one free electron. Such an atom interacts with other atoms and molecules, mostly damaging them. It comes to chromosomal breakage, enzyme inactivation and membrane damages. Example: A large number of radiology- pioneers, like x-ray explorers, got cancer of the lung or of the lymphatic tissue. Also today, the radiology is not without problems: X-ray of the breast must be made with soft radiation to prevent the tissue of damages. All x-ray diagnostics must be well documented to prevent patients from a high dosage by multiple x-rays in a short time period. (13)

III. Viral Carcinogens
A virus is an infectious particle, consisting of a capsule and a core with the genetic material. It is a cellular parasite, which needs another living cell, to transfer his genetic material into and reproduce it. Such an infection can cause an oncogenic impact (genome deregulation) during the genome transfer, by one of the following mechanism: The viral genome can form stable associations with the human cell genome, it can be translated into the human genome (retroviruses translate their RNA into the human DNA and implant it into the human genome, the viral genome is then involved into cellular mechanism like growth), or the viral genome products bind cellular proteins and affect the signal transduction (f.e.: cancer supressor inactivation). Today, the following viruses are known as linked with human cancer:
Epstein- Barr virus (EBV) - can induce Nasopharyngeal Carcinoma and Burkitt Lymphoma,
Human papilloma virus (HPV) - can induce Cervical cancer, Skin and Larynx Papilloma,
Hepatitis B virus (HBV) - can induce Hepatocellular Carcinoma,
Human T- cell leukemia virus (HTLV-1) - can induce a T- cell leukemia. (8, 11)

IV. Bacterial Carcinogens
Although the implication of bacteria in the development of cancer is not as well explored as the other carcinogens, one possible explanation of the bacterial cancer induction is the chemical modification of food components by an abnormal bacterial flora:

Some saccharides, fats and proteins can be activated by "unfriendly" bacteria into carcinogens, f.e.: the bacterial degradation of protein and urea leads to an increase of ammonia. Vaginal bacteria can act similar to this, producing carcinogen nitrosamines and free radicals during a vaginosis infection, what can lead to cervical intraepitelial neoplasia. Such a condition when unfriendly bacteria have a more powerful presence in the gastrointestinal tract or vagina because they outnumber friendly bacteria is called Disbiosis. Disbiosis can be induced by infection, antibiotics (which can kill the normal and friendly bacteria), and an wrong diet. The friendly bacteria, like Lactobacillus and Bifidobacteria species, live in symbiosis with host (human organism), protect host tissue and resist colonization by exogenous unfriendly bacteria: First, their presence creates a competition for substrates, so the unfriendly bacteria have problems to colonize and to cause an inflammation or produce carcinogens. Second, they seem to have a direct effect on mucus secretion, which protects the tissue from infection and substance damage (f.e.: by radicals). Example:
Helicobacter Pylori infection can result in a B- cell lymphoma of the mucosa associated lymphatic tissue.

2.2. Promotion

After the initiation (genome impact), the next step in cancerogenesis is promotion. Promotion means that the genome damage, set in the initiation period, could not be repaired, and is now going to be multiplied to daughter- cells. Typical for this step of cancerogenesis is an increase of clonal cell growth. Cancer promoting agents are similar to carcinogens, in some cases identic, increasing the cell growth by causing an alteration of cellular interactions, components, or functions important for a controlled cell growth. Examples:
Chronic irritations - cause an increase of tissue repair, growth and adaptation mechanisms. If some cells acquired an initiating genome alteration, this alteration can be multiplied to daughter cells. It is also important to know, that a cellular adaptation to chronic irritations (can be also a result of chronic infections) often causes a change or decrease of differentiation in altered cells (the first process is called Metaplasia, the second Dysplasia).
Phorbol esters - (croton oil components) show the following effects: First, they activate protein kinase C, a cellular signal transduction protein (see chapter 2.1. initiation) and proto- oncogen, what can initiate the process of cancerogenesis. Second, they promote the cancerogenesis by a stimulation of the enzyme ornithine decarboxylase, known as necessary for mitogenesis. (17) Third, they promote the cancerogenesis by an interference with the gap junctional intercellular communications (see the image Nr.3):

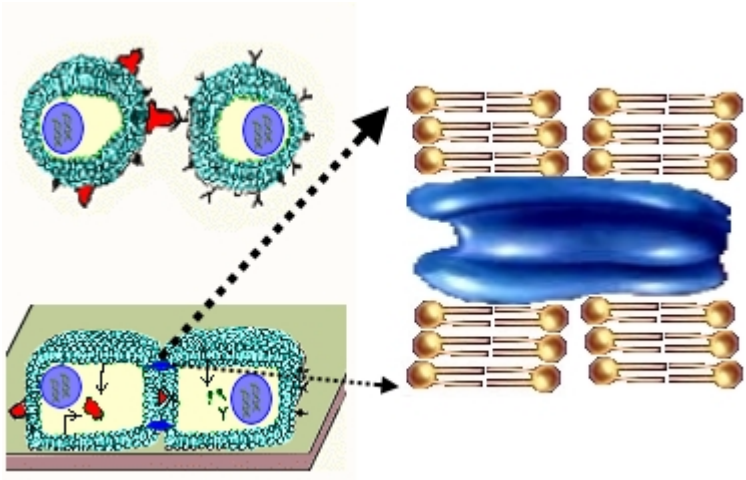


Image Nr.3 - Gap Junctions and Contact Inhibition

Contact inhibition means, that a cell stops growing in a tissue when it gets contact to another cell. The upper left part of the image shows a contact of two cells. Both have adhaesion molecules and receptors (red, black) at the outer cell membrane. In case of normal growing epithelial tissue, such cells form a monolayer (left inferior image part), caused by the orientation of cellular contact structures at the outer membrane (black arrows). The further communication between cells in a tissue is provided by gap junctions (blue)- channels between two cells, which consist of molecules, called connexons. The right image part shows such a gap junctional channel. When all cells are connected together by gap junctions, they act as one functional system. The regulation of controlled cellular activity as well as the controlled cell death (see chapter 2.1.4.apoptosis) seems to depend on gap junctions. A block of this structures, for example by Phorbol esters, causes a decrease of cellular communication and controll, and is promoting the process of cancerogenesis: The most important characteristic of cancer cells is their independent, uncontrolled growth.

2.3. Progression

This is the final step in cancerogenesis, when a number of cells grow to a visible cellular mass, called tumour. This tumour has all the characteristics mentioned in the chapter 1.2. Malignant Neoplasia. Factors like immune system response, localization, blood support and the rate of growth, play an important role in this process.

During the change of differentiation in the canerogenesis, cancer cell can present new or modified antigens on the outer cell membrane. This antigens are cell type-, tissue- and species-specific molecules, which can identify the cell to other cells and to immune system. Example: The MHC I (Major Histocompatibility Complex), found at the outer membrane of most human cells, can present protein structures built in the cell to the environment. If a cell is producing false proteins (in case of neoplasia or virus infection, due to the genome change), this proteins will be presented with the MHC I to cytotoxic T- lymphocites. This T- cells are specialized in killing foreign cells, due to their foreign antigen structures. Other special lymphocites can activate Macrophages (specialized in killing by digestion) and NK cells (natural killer cells), or produce antibodies (proteins that recognise antigens, produced by B- lymphocites) which mark a tumour cell like a targed for the immune system. An immunodeficiency, seen f.e. by AIDS patients, is in connection with a higher incidence of malignant tumours. Under special circumstances a cancer cell can stay alive also in a body with normal working immune system (mechanism called immunosurveillance): First, a malignant cell can mask its outer antigenes, f.e. by a produced or already existing substance like fibrin. Second, malignant cells can produce and excrete molecules, which act as an antigen, overload the organism and exhaust the immunity system. Third, they can excrete molecular signals, which suppress the activity of the cellular immune system.

The growth rate has the following influence on tumour progression: First, a fast growing tumour can compress the normal tissue in the neighbourhood, sometimes causing a cell death. The cell death is always followed by a (small) immune reaction with an increase in concentration of immune cells in the tumour area. The immune cells can affect the further tumour progression. Second, the fast cell growth can only progress, as long as the nutrition support (blood) is guaranteed. A fast growing tumour can compress vessels or grow too fast so that there could be a relative decrease of vascular support in the tumour area. The most fast growing tumours have a centre consisting of dying or dead cells due to this nutrient defficiency, but there is also a small amount of (slow growing) tumours which produce angiogenesis factors (factors increasing the vessel growth), which grow with a normal nutrition supply.

2.3.1. Metastasis

Some cancer cells can spread locally or through the bloodstream and lymphatic system to other parts of the body, depending on cancer type and location. Like most other cellular mechanisms, also the metastasis seems to be initiated by an activation of genes.

Example: An alteration of the NM23 gene at chromosome Nr.17 was found in metastases of colon cancer, brast cancer and melanoma. The normal NM23 gene is a potent supressor of metastasis activity in cells. Another genetic mechanism seems to decrease the expression of cell adhesion molecules, which are implicated in binding and attachment of the cell to other cells or to the basement membrane. Reduced expression of this cell adhesion structures allows detachment of tumour cells from the parent tumour, what can lead to a local metastasis. To spread in further areas, the tumour must destroy the basement membrane by secretion of proteolytic enzymes and invade through deeper tissue layers the blood or lymphatic vessels. The movement through the intestinal tissue can be increased, when tumour cells produce autocrine motility factors which stimulate the cell movement. The activated cells can form moving eminences (pseudopodia) which act like small legs. By a destruction of vessel basement membrane, they can get into a vessel and spread into further areas of the body. There are following types of metastasis:

I. Cavity Metastasis
This is a tumour spread in anatomic caves. Example: Gastric cancer can perforate the stomach wall and fall into the abdominal cave, spreading into the innner female reproductive system (Ovarial metastasis, known as Krukeberg tumour).

II. Blood Metastasis
This type of metastasis is often seen in malignant sarcoma tumours. Location of the primary tumour plays an important role in this mechanism (see image Nr.4). Location of the metastasis depends also on the organic vessel denseness and diameter. Some organs, like the lungs, liver and brain, act as a natural filter due to their vascularisation. Examples: Bronchial carcinoma (lung cancer) metastasis spread through the large body circulation into the bones, brain and liver. Hepatocellular carcinoma (liver cancer) metastasis spread through the liver vein into the lungs. Kidney and Bones metastasis spread through the large vein (v. cava) into the lungs. Most intestinal tumour metastasis spread through the portal vein into the liver.

III. Lymph Metastasis
This type of metastasis is often seen in malignant carcinoma tumours. Lymph vessels so not have a basement membrane, so their infiltration by tumour cells is not as difficult as the infiltration of blood vessels. A malignant tumour can spread through this vessels, or it can grow into them (called Lymphangiosis carcinomatosa). In case of a tumour spread, the first filters are lymph nodes, which are also the first target of metastasis. The process of metastasis can stop at this point, or the growing tumour metastasis can erode the node and spread through the large thoracic duct (large lymph vessel, connecting lymph and draining it into the right and left subclavian veins in the thorax) into blood vessels (8, 18, 19) , further acting as a blood metastasis (into the lungs).

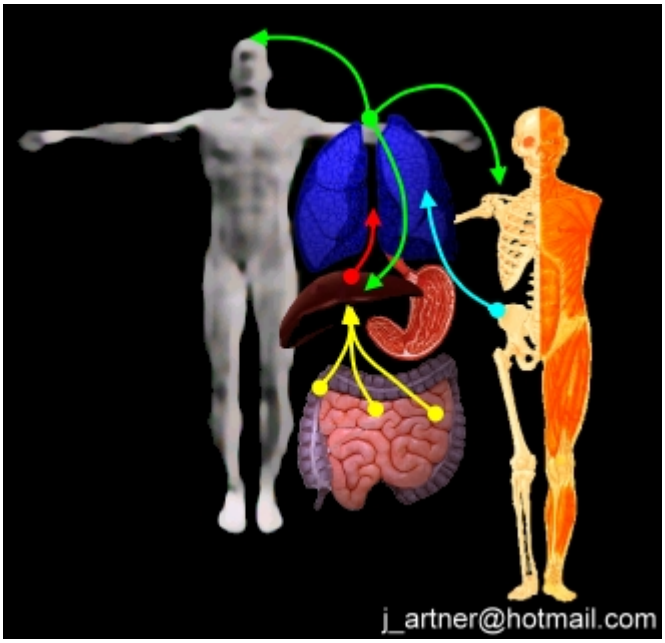


Image Nr.4 - Blood Metastasis
This image shows the most common types of blood metastasis. Green arrows represent the spreading of a bronchial carcinoma into the brain, bones and liver. Red arrow represents the hepatocellular carcinoma (liver cancer) metastasis spreading into the lungs. Blue arrow represents the bone tumour metastasis into the lungs. Yellow arrows represent the spreading of most intestinal cancers into the liver. A change of the metastasis type and target location is possible in theory, but rare (f.e.: All deeper located tumours, like intestinal and genital, should spread into anatomical filters, intestinal into the liver and genital into the lungs but it happens in some cases, that a genital tumour- cell gets out of such a filter and spreads into the brain.).

3. Cancer Risk Factors and Predisposition

There are some environmental, genetic and behavioral factors, which increase the risk of a tumour dissease:
diet
tobacco
infection
sexual behavior
occupation
alcohol
geographic factors (20)
age factors
inherited conditions

3.1. Dietary Factors

This factors include the eating behavior and the diet components. How important this factors are, shows the following citation from The American Institute for Cancer Research: "As many as 375,000 cases of cancer, at current cancer rates, could be prevented each year in this nation through healthy dietary choices". (21) The cancer risk can be reduced by changing the individual eating behavior, for example by eating less salty meat, less fat and more fruits.
The exposure to carcinogenic diet components can be reduced by knowledge and prevention. Most carcinogens found in food were already listed in the chapter 2.1.5. (Chemical Carcinogens), but we will desribe them for a better understanding one more time, with focus on the diet:

I. Broiled Meat
Polycyclic aromatic hydrocarbons are chemical carcinogens with a ring systems formed by the incomplete combustion of organic material like coal. They are present in high concentrations in charcoal- broiled meats, deposited on the surface during cooking. They could be, together with salt, responsible for the increased incidence of stomach cancer in Japan population. Non diet related cancers, resulting from a high aromatic hydrocarbons consume or contamination are cancer of the lungs, skin cancer and scrotal cancer.

II. Salt
Asian children, who eat a grat deal of salty fish tend to have high rates of cancer of the nasopharynx and stomach. There is no laboratory evidence that normal salt is a carcinogen, it is more likely that a combination of salt, nitrate and other components, used for the preparation of a special japanese fish meal, may be carcinogen. (22)

III. High Fat Content
High fat content of diet could be a propable factor for the increased rate of colorectal cancer. Some possible explanations for this could be: First, fatty acids are essential components of every cell membrane. Animal studies show that depending on the type of dietary fat, they could induce changes in cell membrane lipid composition and proliferation in the colon cells and these changes may be related to the development of tumors. (23, 24) Second, fat causes an increase of bile acids secretion. High amount of bile acids, especially deconjugated bile acids (by some intestinal bacteria), is toxic to the colonic epithelium and cause diarrhea. Bile acids or their metabolites appear to be toxic to enteral cells and are thought to contribute to the development of colon cancer and to ulcerative colitis, a dissease which is often associated with a high colon cancer risk. (25, 26) Third, some fatty acids could also become toxic by heat modification. Unsaturated fatty acids are very reactive because of their double bonds. Their destruction by heat could cause an increase of free radicals (see chapter 2.1.5. Physical Carcinogens). Fourth, some fatty acids (arachidonic and linoleic acid) are precursor molecules to eicosanoids, a group of hormone- like substances: Depending on the biochemical pathway (enzyme cyclooxygenase/ lipooxygenase), these fatty acids can be metabolized to prostaglandins, leukotriens or thromboxanes. Prostaglandins and leukotriens have an influence on the immune reactions thru cell stimulation. Research data suggest that some of them may have an influence on cell growth and cancer promotion and that an innapropriate production of these eicosanoids may represent a link between dietary fatty acid intake and cancerogenesis. (27, 28) Fifth, high fat intake causes a gastroesophageal reflux (f.e. thru CCK hormone signals). This backward- flow of gastric acids causes a chronic irritation of the esophageal tissue, which can change its differentiation for protective reasons (Metaplasia). Such a change of differentiation is often linked with a higher cancer risk and the metaplastic esophagus is called Barett Esophagus.

IV. Low Fiber Diet
Fiber seems to have a cytoprotective effect on intestinal cells. Possible reasons for this effect are: First, fiber moves food more quickly through the intestines and cancerogens could be elimineated faster by this mechanism. Second, fiber draws water into the intestinal tract and this could dilute carcinoges and decrease their effect on the intestinal cells. Third, fiber may bind with toxic bile acid products and eliminate them from the intestines. Natural sources of fiber are vegetables, beans, whole grains and fruits. (26)

V. Alcohol
See the chapter Alcohol.

VI. Hot Beverages
It is possible, that drinking hot beverages could increase the risk of esophageal cancer. Hot beverages could cause a chronic irritation of the esophageal tissue, which could become metaplastic (cellular adaptation by change of cell differentiation).

VII. Aflatoxins
This are toxic substances, produced by Aspergillus flavus and Aspergillus parasiticus (fungi). The contamination of seed and food (like corn and peanuts) occurs due to poor food harvesting or storage practices. Aflatoxins are known human carcinogens, which can cause (after bioactivation by liver enzymes) liver cancer.

VIII. Other Factors
Although not all dietary carcinogens can be described due to a lack of space, it should be finally two important dietary factors mentioned: First, there are food components, used as color enhancers or preservatives, which can increase cancer risk (by forming N- nitroso compouns). Second, an incomplete combustion of polycyclic aromatic amines during cooking can also increase cancer risk. Aromatic amines are created by the reaction of sugars, amino acids and creatinine in muscle meats (beef, pork, lamb,..). (17)

3.2. Tobacco
Its a well known fact that tobacco smoke contains carcinogens like polycyclic aromatic hydrocarbons and N- nitroso compounds, which cause cancer of the lungs, upper respiratory tract, esophagus, bladder and propably of the stomach, liver and kidney. Altrough this facts are well known, many people cannot or don't want to give up smoking because of addiction.

3.3. Infection
Like already mentioned, a chronic inflammation and irritation can cause cellular adaptation in the form of a differentiation change. Infections and inflammations, known for their possible connection with cancer are ulcerative colitis (chronic inflammation of colon), Helicobacter Pylori infection (can cause gastric cancer or malt lymphomas), Epstein- Barr virus infection (nasopharyngeal carcinoma or Burkitt lymphoma), Human papilloma virus infection (can cause cervical cancer, skin and larynx Papilloma), Hepatitis B virus infection (can cause hepatocellular carcinoma) and Human T- cell leukemia virus infection (can cause T- cell leukemia). (see chapter 2.1.5. Carcinogenic Agents) (29, 30)

3.4.Sexual Behavior
The risk of genital and breast cancer also seems to depend on factors like amount of sexual partners or intercourses, age of starting sexual intercourse, amount and age of pregnancies, type of sexual practice, use of contraceptives and the hygiene status. These factors can cause cancer by one of the following mechanisms: viral or bacterial infection (see chapter 3.3. infection), chronic irritation or damage of tissue, and hormonal disbalance (of sex hormones). (29)
Examples:
An early onset of sexual activity and high amount of sexual partners increase the risk of cervical cancer. It is possible, that the increased irritation of inner genital tissue causes adaptation mechanisms like metaplasia, which can result in cancer. A low hygiene status can also increase, together with the previous factors or alone, the vaginal, anal or penile cancer risk because of viral and bacterial contamination, infection and irritation. In the same way also anal intercourse of homosexuals increases the risk of genital cancer. Most important viral carcinogens, which can be transmitted by sexual intercourse, are Human Papilloma virus, Herpes Simplex virus and Cytomegalovirus. Althrough bacterial infections of the genital system (caused by genera Trichomonas, Neisseria, Shigella, Campylobacter,...) are not as important as the viral infections, they can cause a chronic irritation and can increase the risk of cancer too.
Having children early in life may have a breast cancer protective effect by the following mechanism: Breast cells are under the influeance of sexual hormones, which cause their differentiation. A first pregnancy at a young age causes this differentiation earlier and the breast cells are much less susceptible to carcinogens.

There is some evidence, that the use of oral conraceptives can increase the risk of breast, cervix and liver cancer. This occurs, with the exception of liver cancer, through a hormonal disbalance and the resulting cell stimulation by sexual hormones (estrogen, progesteron). (31, 32, 33, 34)

3.5. Occupation

There are occupations which can increase a human's exposition to carcinogenic agents, like mine worker (exposition to subterranean radiation), farmer (solar uv- radiation), chimney sweep (coal and tar exposition) or a physician (x-ray radiation). Examples: A high exposure to solar radiation is a predisposing factor to skin cancer. Exposure to coal and tars can cause scrotal or lung cancer. (8, 29)

3.6. Alcohol

There is an association between alcohol use and increased risk of cancers of the esophagus, pharynx, mouth, liver and colon. The active component of alcohol is ethanol, which is transformed into acetaldehyde in the liver (catalized by enzyme alcohol dehydrogenase). Alcohol can promote cancer by the following mechanisms: First, alcohol components are able to induce the liver enzyme cytochrome P-450, which is involved in the bioactivation (helps to detoxify substances, but under some circumstances, this mechanism can activate a substance into a carcinogen) of substances. Due to this enzyme induction, some carcinogens (f.e. from tobacco or diet) can become more potent. Second, acetaldehyde, which is a product of alcohol metabolism, could affect the natural cell genome repair mechanisms and induce a catabolic metabolism (f.e. digestion of cellular proteins). Third, a high concentration of ethanol can cause erosive gastritis in stomach, which is associated with an increased cancer risk. Fourth, chronic alcohol abuse may result in a lack of important and protective food components like vitamin E, B and A. Example: Chronic alcohol abuse results in an accumulation of ethanol and some of his toxic metabolites in the liver. The lack of protein components and enzymes (because of the catabolic effect) and the toxic damage cause a cell degeneration (the liver cell is full with fat and the functional structures are repressed because the lack of intracellular space). Because of the lack of functional structures (f.e. detoxifying structures), it comes understandably to a self-perpetuating destructive process (alcohol or toxic substances reach the liver but the detoxifying enzymes are exhausted) what can result in a hepatitis (liver inflammation) or liver cirrhosis (lost of functional liver structures, anatomic architecture and replacement of normal cells by fibrous tissue). In this example all steps increase the liver cancer risk because there is a chronic irritation, inflammation and susceptibility to toxic and carcinogenic agents. (8, 35, 36)

3.7. Geographic Factors

Geographic Factors have an influence on exposition to radiation, viral carcinogens and on the nutritive habits. Example: The increased exposition of Australia's population to uv-light is the reason for a higher incidence of skin cancer. High pigmentation of the black population has a protective effect.

3.8. Age Factors

Many cancer types occur at a specific age period, which determinates specific organ susceptibility, speed and potence of genome repair mechanisms, preiod of exposure to carcinogens and hormonal level. Most cancer types (like cancer of colon, lungs or breast) occur at higher age, because of longer exposure to carcinogens, slower genome repair mechanisms and weaker immunity. There are also some types of cancer, which have an increased incidence in the childhood, like cancer of the brain and spinal cord, bone, leukemia (cancer of the white cells, responsible for immunity), neuroblastoma (neural origin), retinoblastoma (malignant eye tumour), Wilms tumour (cancer of the kidney) and rhabdomyosarcoma (originates in skeletal muscle). In United States, one in every 330 children develops cancer before the age of nineteen. The causes of most childhood cancers are not yet known, but there may be an increased risk if childhood cancer in children who have a genetic condition (f.e. Down syndrome, when an infant is born with three copies of the 21st chromosome).

One possible reason for the childhood's increased incidence of neural (and other) cancer types could be a low differentiation of the organ tissue (f.e. brain, spinal cord, muscle, althrough they are differentiated, they grow also after birth) or the high growth rate of tissue (more susceptible to carcinogens). (8, 37, 38)

3.9. Inherited Conditions

Some of the inherited malignant tumours were already mentioned as childhood cancer in the previous chapter (retinoblastoma, Wilms tumour). There are also inherited benign tumours like the familiar polyposis of the colon, which increase the risk of a malignant tumour transformation. Inherited genetic defects, like Down syndrome, also increase the risk of cancer. Some cancer types, called family cancers, show an amassment within a family, like the breast cancer and colon cancer, but the hereditary predisposition to them is not clear. (8, 29, 39)

4. Effects of Tumour on Host

The effects of tumours can be divided in local effects (affecting a body part, vessel, duct or other), systemic effects (affecting the whole body) and paraneoplastic syndromes (symptom complex, which cannot be explained by local or distant spread of the tumour, but can be explained by ectope hormone production of tumour cells):

4.1. Local Effects

Local tumour effects on host are result of fast local tumour growth, ischeamia (low blood and oxygen supply) or destruction by tumour. A tumour can erode vessels or a tissue which contains a large amount of vessels, resulting in a bleeding. A fast growing tumour can compress vessels and cause a local (in case of large vessels systemic) ischaemia or cell death, resulting in a tissue destruction. A tumour can compress a duct or obstruct it and cause a secretion block. Tumours also can compress nerve fibers and cause pain. (8, 40, 41)

4.2. Systemic Effects

Systemic effects are result of homonal level changes, changes of blood supply or blood components. Most common effects on host are cachexia, fever, hormonal effects and anaemia:

4.2.1. Cachexia

Cachexia is also called wasting syndrome, which is characterized by weight loss, loss of appetite, weakness, impaired wound healing (because of protein loss), and anorexia. Althrough most tumours have an high metabolic turnover (due to anaerobic glycolysis, which causes an increase in nutritional needs), this mechanism alone seems not to be responsible for the symptoms of cachexia. There is some relation between a substance, called cachectin, and the symptoms: Cachectin is used synonymous with tumour necrosis factor alpha (TNF-alpha), which is produced by macrophages, T- cells (CD4+ helper class) and natural killer cells after their stimulation. Additionally, some muscle cells (smooth muscle), neutrophils, some brain cells (astrozytes) and a variety of tumour cell lines can produce cachectin (TNF-alpha). (41, 42, 43)

4.2.2. Fever

Fever is usually the result of tissue necrosis (cell death) or infection. A fast growing tumour often causes cell death (tissue destruction due to invasion, vessel compression,...), what again causes immune response, f.e. by macrophages (cells which are specialized in digestion of material and cells). This macrophages communicate with the environment through cytokines (hormone- like substances) like Interleukin 1, which stimulate other immunity cells and which is the central mediator of fever. Interleukin 1 causes in the preoptic anterior hypothalamic region of the brain a misadjust of body's target temperature value, resulting in a higher body temperature. (29, 40, 44)

4.2.3. Hormonal Effects

Some benign tumours can cause in the tissue of origin an increased hormone production. Example: B cell adenoma in pancreas can produce higher amount of insulin which is responsible for the sugar balance. Increased levels of this hormone in blood cause high intake of sugar into cells what again lead to a lack of sugar in blood (called hypoglycemia). Since sugar is responsible for energy supply, a lack of this essential component causes weakness and other cachexia- like symptoms.

4.2.4. Anemia

Anemia stands for state with a lack of blood or blood components (mostly red blood cells). It is caused by blood loss, malnutrition or underproduction. Example: Gastric cancer can erode stomach's walls and cause a chronic bleeding. This blood loss may cause an anemia, resulting in a pale, colorless skin, loss of concentration, unconsciousness, difficulty in breathing, shock and in worst cases death. Another example: Esophageal cancer can obturate the duct and make a normal food intake impossible. The resulting lack of essential food components like vitamins, aminoacids or iron causes a lack of red blood cell's component parts, which cannot be built in bone marrow without all essential components. The result is again an anemia.

4.3. Paraneoplastic Syndrome

Sometimes it occurs that a hormone or hormone- like substance is produced by a cancer, which is not usually produced by the original tissue. Such a unusual hormone production is called ectope hormone production and the resulting symptoms are summarized in the term paraneoplastic syndrome. Paraneoplastic syndromes are observed by 15 percent of all cancer patients. Examples:

Breast carcinoma cells may produce calcitonin hormone and cause a hypocalcemia (lack of calcium), resulting in spasm or loss of concentration.

Kidney cancer cells may produce erythropoietin hormone and stimulate a massive growth of red blood cells, resulting in an increased risk of thrombosis (vessel obturation) and infarction. Although a production of erythropoietin is also naturally localized in kidney and this example could be misplaced, there are only a few specialized cells in normal kidney which produce this hormone.

Lung cancer cells may produce ACTH hormone (adrenocorticotropic) and stimulate adrenal gland, resulting in an high secretion of adrenal hormones like cortisol which may cause Cushing's Syndrome (weakness, fatigue, depression, mood swings in combination with weight gain of face, neck and upper back, thinning and weakness of muscles of arms and legs, thinning of skin, acne, scalp hair loss or skin darkening).

Some sarcomas can produce isulin- like hormones and cause hypoglycemia (similar mechanism is described in chapter 4.2.3. Hormonal Effects). (8, 40, 41)

5. Cancer Therapy

Although cancer is the killer number two (after cardiovascular disease) worldwide, it is important to know that the diagnosis "cancer" does not mean a death sentence. There a many ways, medical, complementary and alternative, to fight cancer. The treatment method depends on factors like patients state of health, rate of cancer growth, cancer type, existence of metastasis and localization of tumour or metastasis. There are two different types of treatment intentions, palliative (to prolong life and soothe down the pain) and curative (to eliminate all cancer cells), both using similar treatment methods but in different intensity. We will focus on the medical curative treatment methods now and describe some alternative methods later:

5.1. Medical Cancer Treatment

This type of treatment is scientifically tested and aproved. There are five treatment options: Surgery, radiation therapy, chemotherapy, hormone therapy and immunotherapy, which can be also used in combination.

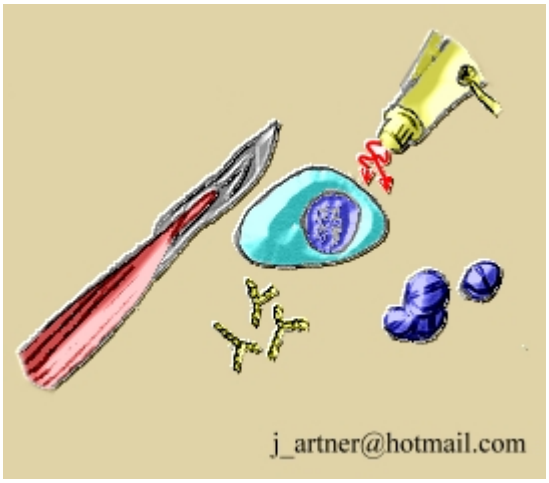


Image Nr.5 - Medical Treatment
This image shows the most common medical types of cancer treatment:

Surgery (red scalpel)
Radiation (yellow machine)
Chemotherapy (blue pills)
Hormone Therapy (blue pills)
Immunotherapy (yellow antibodies)

5.1.1. Surgical Treatment

Surgery is the oldest form of treatment. The primary intention is to remove all cancer cells from host. This is only possible, if tumour mass is solid or encapsulated. The surgeon removes the tumour as well as some of the (normal) tissue around the tumour. This tissue is sent immediately to the pathologist who looks if there are no microscopic parts or cells of the tumour. It is sometimes unavoidable that the surgeon removes also lymph nodes near the tumour. This is a preventive measure because of possible early metastasis. It is possible, that the surgical treatment is combined with radiation therapy or chemotherapy, before or after surgery. (8, 13) Side effects of surgical treatment are rare, but following examples of most common side effects should be mentioned: The lack of lymph vessels, if they were removed, can cause a local edema. Another possible problem could be a surgical cut into a tumour with a high vascularity (high amount of vessels), what could result in a massive bleeding. A vessel injury and bleeding also increase the risk of thrombosis and embolism. (51)

5.1.2. Radiation Therapy

Like already mentioned (chapter 2.1.5 Carcinogenic Agents), radiation can cause cellular (mostly genetic) damage, mutation or death, depending on the radiation intensity. If the radiation intensity is high, the cellular and genetic damage on a cell is lethal. This damaging effect is used in the radiation therapy for killing cancer cells. The radiation can be given external or internal, depending on the localization, rate of growth, metastasis and size of tumour. The internal radiation therapy implants or places small source of radiation into deeper parts of the body or into a cavity. The external radiation is given by a machine (f.e. linear accelerator) and can be used for radiation of superficial and deeper localized cancers. After the initial consultation, the radiation is planned and simulated: The exact localization of tumour is discovered with x- rays or computer tomography. A sign on the skin can be drawn to identify the patient's treatment area. The machine settings for the radiation can be simulated with non-damaging lasers or similar and the settings are written down for the real treatment session. The modern medical radiation devices can focus on a very small target, producing a heavy, damaging radiation and prevent normal tissue from damaging radiation by their thin rays and protective shields. There can be some temporary side effects, which depend on the radiation-area and the dose. The most commmon side effects are skin reactions (skin can become red, dry, irritated or sensitive in the area), weakness (most common side effect), hair loss in the area of treatment (depending on the dose) and enteral problems like atered taste, diarrhea or vomiting (due to alteration of gastrointestinal, esophageal or tongue cells). It is important to be aware of the preventive mechanisms (focus on small target, simulation, shielding) because of the misleading prejudice that radiation therapy causes a loss of scalp hair or that a patient can become radioactive.

First, with the exception of radiation treatment of head tumours, there is no loss of scalp hair due to radiation therapy in any body part. Second, the patient who gets external radiation is not radioactive. Patients with internal radiation sources can show small radiaoctivity and have to stay in hospital during the treatment period. (13, 45)

5.1.3. Chemotherapy

The term chemotherapy is used for treatment methods which use cytotoxic drugs (cyto means cell, toxic means poison) and substances. All growing cells are going through a cell cycle. A simplified cell cycle would start with an increased production of cellular structures like proteins and enzymes, followed by a replication of genetic material. After this material (genome) is doubled, every genome copy is moved to each cell pole and the cell starts to divide. After this simpified cell cycle there are two daughter cells with equal genetic material. Almost every step of this cell cycle can be altered or stopped by chemical substancies by following mechanisms:
Alkylation of genetic material - causes stable bonds in genome and the genetic material cannot be replicated (doubled). This mechanism is seen in drugs like cisplatin, busulfan and cyclophosphamide. (46)
Enzyme inhibition - causes a stop of replicating enzyme activity. This mechanism is seen in drugs like lomustine and carmustine.
Mitosis protein inhibition - causes a stop of the polar genome movement (before division) and division due to an alteration of intracellular movement proteins (f.e. microtubuli). This mechanism is seen in alcaloid drugs like vincristine, vinblastine and paclitaxel.
Component competition or false components for genome synthesis - cause, after their implantation into genome (because of their similarity to normal genome components), production of false or irreplicable genetic material. This mechanism is seen in drugs like 5-fluorouracil and cytarabine.
The mentioned mechanisms affect all fast growing cells in the body, fast growing normal cells included (bone marrow tissue, intestinal tissue, reproductive system, hair follicles, ...), what may result in a couple of side effects: Bone marrow (produces blood cells) supression can result in low white blood cell counts (lower resistance to infection), low red cell counts (fatigue, headaches, shortness of breath, anaemia) or/and low platelet counts (problems to stop bleeding). The possible damaging or irritating effect on intestinal or digestive tissue may cause changes of taste, esophagitis, vomiting or loss of weight or appetite. The damaging effect on hair follicles may cause a loss of hair. There are also some other effects, like infertility, allergic reactions, lethargy and changes in nervous system, but most effects are only temporary, during the treatment period. (47, 48, 49)

5.1.4. Hormone Therapy

Hormon- like drugs are used to supress the growth of certain hormone- dependent cancers. Such drugs include estrogens, antiestrogens, progesterones, adrenocorticosteroids and androgens. Example: Tamoxifen can be used for the treatment of the estrogen- dependent breast cancer.

5.1.5. Immunotherapy

Immunotherapy is a form of treatment which helps the immune system to identify, attack and destroy cancer cells. For this purpose specific cancer antibodies or immunity stimulating hormones (cytokines like colony stimulating factors for a cell population, interleukins or interferones) are produced and given to patient. It is possible to attach cellular toxins to cancer-specific antibodies (immunotoxins), which then better and faster find their way into a cancer cell.

5.1.6. Other Medical Therapies

This are therapies, which do not fit into any previous chapter and are often used in combination with other therapies like radiation. Examples:
Bone marrow transplantation is used for the treatment of leukaemia and is given after a short radiation therapy period.

Bone marrow cells can come from the same person (autologous donation), when cells were collected, isolated and stimulated to grow, or from other person (allogeneic donation) if the cells from donor are compatible to acceptor's cells.
Heat therapy is can be used for the therapy of superficial tumours in combination with radiation therapy. The mechanism of this therapy is that an increased temperature in the tumour area makes it more susceptible to radiation (most chemical reactions are faster when temperature is increased, forming of free radicals included). (13)

5.2. Complementary and Alternative Cancer Therapy
First, the two terms should be explained and differentiated: The term alternative therapy is used for a unproven (scientifically) therapy instead of standard medical therapy. An alternative therapy has has not been scientifically tested or approved and it is not a substitute for the standard medical therapy. Complementary therapy, on the other hand is used in addition to standard medical therapy and can be helpful for the treatment of some cancer symptoms. Examples for a complementary therapy are meditation, or tai chi (reduction of stress), acupuncture or massage therapy (reduction of pain), of course in combination with standard treatment. Although complementary methods cannot cure cancer, they are a good and important support. (50)

6. Classification of Neoplasms
Every tumour has a special name (nomenclature), depending on the tissue of origin, dignity (benign or malignant), microscopic appearance, and sometimes on the discoverer. The name alone is not enough for a cancer treatment, it is also important to describe cancer's behavior like the size, spead, metastasis and the grade of cellular differentiation. This classification of behavior is made by grading and staging.

6.1. Nomenclature of Neoplasms
To understand the nomenclature of a tumour, it is important to know the tissue of origin and tumour's dignity. Most benign tumours have a suffix "oma" following the tissue type, with the exception of lymphoma and melanoma, which both are malignant. Some benign epithelial tumours which form glands or their tissue of origin is glandular are called adenoma. Some of them can also form epithelial elevations and are called polyp (elevation of the inner organ epithel) or pappiloma (elevation of the outer skin). Examples for benign neoplasms (by tissue of origin):
Muscle: - Leiomyoma (smooth muscle, f.e. in organs) or Rhabdomyoma (striated muscle for movement)
Bone: - Osteoma
Cartilage: - Chondroma
Connective tissue: - Fibroma
Fat - Lipoma
Skin - Papilloma (superficial cell layer) or Sweat gland adenoma (deeper sweat glands)
Vessels - Hemangioma (capillary or cavernous, depending on the vessel's calibre)
Some tumours can show a combination of two or more neoplasms (mixed origin), like Fibroadenoma (glandular and connective tissue neoplastic components) or Angiomyolipoma (vessels, smooth muscle and fat components).

Most malignant tumours have the suffix "carcinoma" (epithelial origin) or "sarcoma" (mesenchymal origin, like connective tissue, muscle, vessels, fat). Examples for malignant neoplasms (by tissue of origin):

Muscle: - Leiomyosarcoma (smooth muscle) or Rhabdomyosarcoma (striated muscle)
Bone: - Osteosarcoma (Osteogenic sarcoma)
Cartillage: - Chondrosarcoma
Connective tissue: - Fibrosarcoma
Fat: - Liposarcoma
Skin: - Squamous cell carcinoma (superficial cell layer), Basal cell carcinoma (deeper layer) or Adenocarcinoma (deeper glands)
Vessels: - Angiosarcoma (Hemangiosarcoma)

Interrested readers can visit the International Classification of Diseases (see reference Nr. 52) published by World Health Organisation (WHO) for more specific information on nomenclature of neoplasms. (8, 52)

6.2. Tumour Grading

Tumour grade refers to a measure of how malignant tumour cells are differentiated. A sample tissue is removed by biopsy or during surgery and examined by a pathologist (under a microscope). The grade of differentiation is diagnosed by factors like cell size, cell shape, similarity of cells, number of mitosis (divisions), and similarity to the tissue of origin. Based on these factors, a pathologist commonly describes tumour grade by four degrees (recommended by The American Joint Commission on Cancer): (8, 53)
G1 Well- differentiated malignant tumour (least aggressive behavior in most cases)
G2 Intermediate- differentiated malignant tumour
G3 Poorly- differentiated malignant tumour
G4 Undifferentiated malignant tumour (most aggressive behavior in most cases)

Gx Grade cannot be assessed.
Althrough this is the most used method, there have been developed additional grading methods for many tumours.

6.3. Tumour Staging

The most common method is the TNM- system (tumour, nodes, metastasis), developed by The Union Internationale Contre Cancer (UICC). This classification describes how far cancer has spead anatomically, including cancer's size, lymph nodes involvement, and metastasis (distant spread):
T- classifies the primary tumour's size or invasion
T0- no identifiable tumour in the area
Tis- tumour is not invading the local tissues (called carcinoma in situ)
T1,2,3,4a,4b,4c,4d- tumour has an increasing size and shows an invasion into local tissues (1=low invasion/size,4=high stage of invasion)
Tx- primary tumour cannot be assessed

N- classsifies the nodal involvement
N0- no nodal involvement
N1,2,3 - increased nodal involvement
Nx- regional lymph nodes cannot be assessed

M- classifies the presence of metastasis
M0- no evidence of metastasis
M1- metastasis present
Mx- presence of metastasis cannot be assessed

Example:
T1,N0,M0 is a cancer of small size (3cm or less in diameter), showing low invasion into local tissue, no (lymph) nodal involvement and no metastasis. Cancer has a good prognosis it is possible to remove it by surgery (in case of metastasis could surgical treatment become less effective).

Another system, used by The American Joint Committee on Cancer Staging, divides tumours into stages 0 to 4, using factors similar to the TNM system. (8)

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8. Image Index

Image Nr.1
Artner, J. *Benign vs. Malignant Neoplasia*, separate image parts acquired from the copyright free page http://www.tumorboard.com, Software: PhotoImpact 6, ©Juraj Artner, 2001
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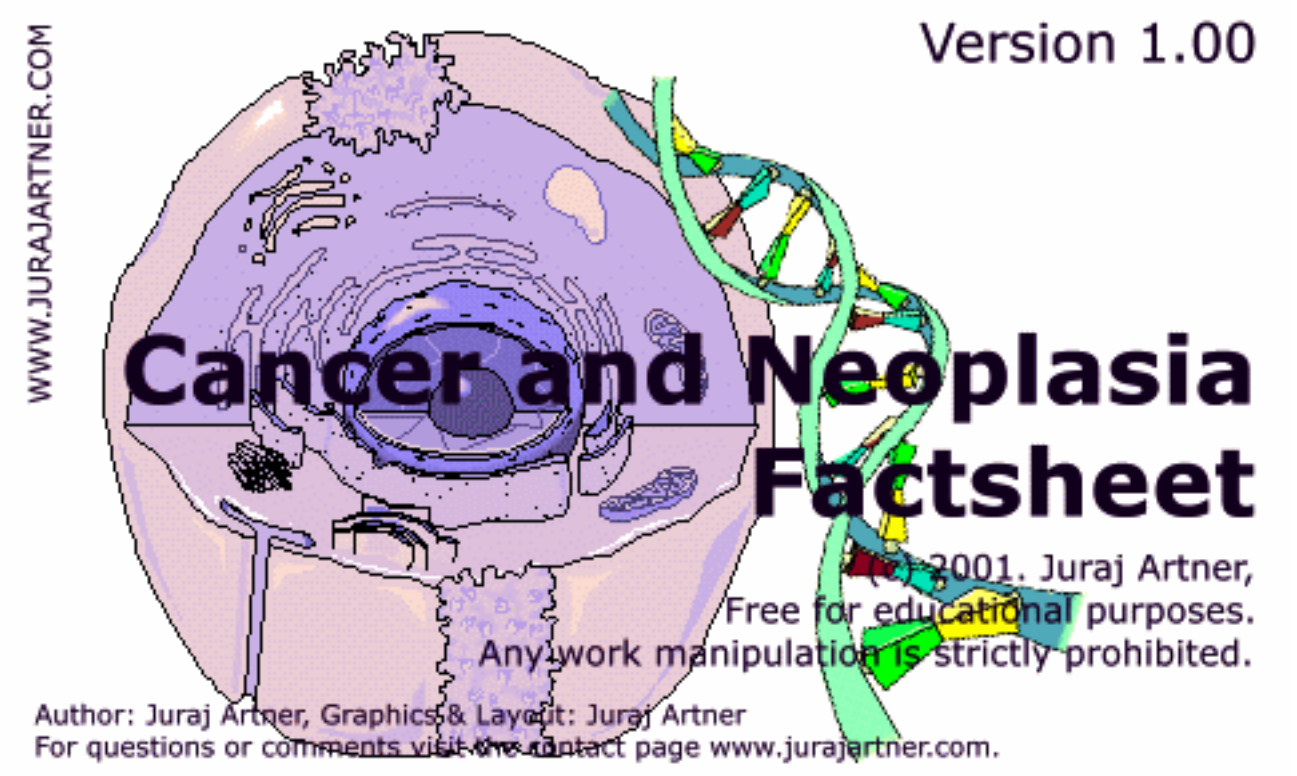

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