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MANUAL

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Tumor is the pathological overgrowth of tissues, which arises spontaneously and is characterized by structural polymorphism and functional independence, these properties being inherited during cell division. Tumors can be cancerous (malignant) or noncancerous (benign). In general, tumors occur when cells divide and grow excessively in the body. Normally, the body controls cell growth and division. New cells are created to replace older ones or to perform new functions. Cells that are damaged or no longer needed die to make room for healthy replacements. If the balance of cell growth and death is disturbed, a tumor may form. Problems with the body's immune system can lead to tumors. Tobacco causes more deaths from cancer than any other environmental substance. Other risk factors for cancer include:

- the living conditions and habits (e. g. such carcinogenic factors as smoking or chewing of tobacco);
- benzene and other chemicals and toxins
- drinking too much alcohol
- environmental toxins, such as certain poisonous mushrooms and a type of poison that can grow on peanut plants (aflatoxins)
- excessive sunlight exposure
- genetic problems
- obesity
- radiation exposure
- viruses. Types of tumors known to be caused by viruses are: cervical cancer (human papillomavirus), hepatocellular carcinoma (hepatitis B and hepatitis C viruses)

Some tumors are more common in one gender than the other. Some are more common among children or the elderly. Others are related to diet, environment, and family history.

At its initial stages a tumor is unlikely to produce any complaints. As the suspicion for a malignancy is sometimes based only on a few indistinct symptoms, the meticulous questioning is mandatory. It is therefore necessary to inquire whether there has been any minor change in the patient's wellbeing. Of great importance is what is referred to as the syndrome of minor symptoms and signs, i.e. the state of discomfort that may be indicative in a malignancy:

- fatigability without apparent cause and a reduction of working capability;
- rejection or unwillingness to eat certain foods
- drowsiness;
- apathy to what used to be of interest;

- «a foreign body» sensation;
- abdominal discomfort rather than pain (e.g. a feeling of heaviness);
- lack of satisfaction after micturition or defecation, etc.

Furthermore, a change in size, colour or consistency of a preexisting lesion (e.g. a birthmark) is not infrequently in a diagnostic value.

Table. Differences benign and malignant tumors

Benign Tumor	Malignant Tumor
Benign Tumor remain in one place as a single well-defined mass of cells; stay together; usually surrounded by a connective tissue capsule; cell structure and function is slightly abnormal	Frequency of cell division in malignant tumor is rapid and completely out of control; cell structure and function is very abnormal; cells of malignant tumor travel to distant sites (metastasize)
Doesn't invade adjacent tissue because of the capsule.	Cells break away to invade surrounding tissues or enter the blood and lymph
Cells of a benign tumor resemble normal cells	Cells don't resemble normal cells
Generally poses no threat to life until they compress vital organs	Malignant tumors become invasive cancer
Restricts the normal tissue's blood supply, affects control centers for heartbeat and respiration	Tumor can spread throughout the body as it travels in body or lymph vessels
Most tumors can be removed by surgery because they are so well contained	Malignant tumor (cancer) shows metastasis and can be categorized according to the types of tissues affected. The treatment depends on the type and stage of the tumor after diagnosis. While some cancers can be cured some of them are incurable. Deadly cancers can still be treated so that patients can live for several years with the cancer.

Metaplasia- is the conversion of one type of adult tissue and/or cells - most commonly epithelia - into another; e.g., squamous metaplasia, in which non - keratinised squamous epithelium replaces ciliated columnar cells in the bronchi of smokers. Metaplasia types:

- Intestinal metaplasia - occurs in the stomach, especially in stomachs that later develop adenocarcinoma.
- Squamous metaplasia - the transformation of glandular or ciliated epithelium to stratified squamous epithelium. In SM of the upper respiratory tract, squamous epithelium replaces ciliated

columnar epithelium; this event, particularly common in smokers, feeds the controversy that this metaplasia may represent a dysplastic process with premalignant potential. Squamous metaplasia of the endocervix is not associated with malignancy.

- Tubal metaplasia of the endometrium - i.e., replacement of the normal endometrial glands with ciliated (fallopian) tubal cells - may occur in endometrial polyps, mild adenomatous hyperplasia and in senile endometrium, but is rarely (and then only coincidentally) associated with malignancy.

Dysplasia - any abnormal development of tissues or organs. An alteration in cell growth resulting in cells that differ in size, shape, and appearance, often as a result of chronic irritation. Examples of dysplasia include epithelial dysplasia of the cervix (cervical intraepithelial neoplasia – a disorder commonly detected by an abnormal pap smear) consisting of an increased population of immature (basal-like) cells which are restricted to the mucosal surface, and have not invaded through the basement membrane to the deeper soft tissues. Analogous conditions include vaginal intraepithelial neoplasia and vulvar intraepithelial neoplasia.

Persistent progression of symptoms is often a hallmark of a malignant condition. The history of the disease is often short in duration; on the other hand, a long-standing chronic inflammation or benign tumor may precede a malignant process. The physical examination is invariably based on routine methods: inspection, palpation and auscultation. At the initial stages patients with malignancy do not show any clinical signs of the disease. Moreover, some may look virtually healthy and even gain body weight. Premalignant conditions include diffuse and focal overgrowth of the epithelium of the skin and mucous membranes, which can be recognized through examination and endoscopy.

The syndrome of pathological discharge (bloodstained discharge or bleeding) can be encountered in advanced stages of carcinoma. Diagnostically, blood-stained discharge is a common sign of malignancy, which is not the case with bleeding.

The syndrome of malfunction is due to structural and functional disorders of the organ involved. Tumors that grow inside, especially those of smaller organs, tend to cause early symptoms of obstruction (e.g. the tumor of the Vater's papilla leads to early development of jaundice). In contrast, when the tumor affects the lumen of a larger organ (e.g. the large intestine) intestinal obstruction is typical of an advanced malignancy. Assessing the functional state of the organ affected the physician has to consider both the functional disorder of the organ and the functional presentation of the tumor itself. Most often, the competence of the organ involved is reduced (e.g. a decrease in the acid output as a result of gastric carcinoma), while the clinical signs of intoxication can be associated with hormonal over activity of the tumor itself.

Pain is not a characteristic feature of tumor, with the exception of tumors arising from blood vessels and neural tissues, which exert pressure on the tissues. Usually, the pain is related to the distention of the adjacent tissues, infiltration of the nerves or organ insufficiency. Hence, intestinal obstruction resulting from the adluminal growth of a tumor causes spastic pains. In

addition, persistent pain suggests either serous involvement or tumorous infiltration of the organ (e.g. tenesmus is a symptom of a rectal tumor).

Palpation is one of the major methods used in the physical examination as it provides the physician with vital information about the tumor. The palpation of the tumor is to be gentle and with appropriate pressure, the fingertips feeling used to feel first the intact adjacent tissue while approaching the tumor itself. It is sometimes performed with both hands, as in the case with feeling the lymph nodes, breast tumors. The size of a tumor measures from millimeters to centimeters. The tumor shape is accounted for by its nature (benign vs. malignant). Modularity of the surface and adherence to the neighboring tissues, coupled with firm consistency, is characteristic of a malignancy, in contrast to a benign overgrowth or a cyst which has smooth surface and is often round and mobile. It is noted that metastatic nodules on the surface of a malignant tumor are likely to be smooth.

The consistency of a tumor appreciably depends on its type;

- soft (normally implies a benign nature of the tumor, e.g. lipomas or polyps of mucous membranes; in some cases, however, this can be a finding of an undifferentiated tumor (e.g. sarcoma);
- hard (associated with an overgrowth of the connective tissue, e.g. fibroma);
- firm (firm consistency, together with elasticity without fluctuation, is typical for an encapsulated tumor filled with fluid);
- wooden-like without demarcation (provides substantial evidence of a malignant overgrowth, i. e. carcinoma). The mobility of a tumor can be either spontaneous (active) or induced (passive).

It is noteworthy that in numerous cases the metastases are identified first. To confirm the diagnosis of a malignant lesion or its metastases, special investigations have to be performed. The following are the examples:

- tumors of the umbilicus;
- tumors of the ovaries (Krukenberg's tumor);
- Virchow's metastasis (the metastasis to the supraclavicular lymph nodes) suggesting gastric carcinoma with distant metastases;
- hepatic enlargement with nodules on its surface in an ascitic patient requires ruling out an abdominal malignant tumor.

To confirm the diagnosis of a malignant lesion or its metastases special investigations have to be performed:

1. Endoscopy.
2. Cytology (swabs, aspirates).

3. Histology (biopsy).
4. X-ray investigations (roentgenoscopy, roentgenography, angiography, lymphography, CT, MRI).
5. Radioisotope methods (scanning, scintigraphy).
6. Ultrasonography.
7. Computerized axial tomography.
8. Laboratory tests (blood cell morphology, enzyme activity etc, as indicated).

One of the crucial points in evaluating the patient suspected of having a malignant disease is the staging of the tumor. It helps decide using the appropriate management.

According to the clinical classification, the four stages of pathological overgrowth are identified:

Stage I — tumor is localized, occupies a limited area, does not infiltrate into the wall of the organ, metastases are absent.

Stage II — tumor is of a big size, can infiltrate into the organ wall but does not spread beyond the organ, there can be solitary metastases to the regional lymph nodes.

Stage III - tumor is of a big size with degeneration, infiltration into the hollow organ wall; multiple metastases to the regional lymph nodes are present.

Stage IV — tumor with distant metastases to organs and lymph nodes and with infiltration of surrounding organs.

Table. The TNMGP classification

Abbreviation	Stands for	Characteristics to be considered	Stages
T	Tumor	Size of the primary tumor	T1-T4
N	Nodes	Involvement of the lymph nodes	<p>NO - nodes are not palpable</p> <p>N1 - metastases to the regional nodes</p> <p>N2 - metastases to the second level nodes</p> <p>N3 - metastases to distant nodes</p>
M	Metastases	Presence of organ metastases	MO - no metastases

			M1 - metastases present
G	Grade	Tumor differentiation	<p>G1 - low level of malignancy (highly differentiated tumor)</p> <p>G2 - moderate level of malignancy (low differentiated tumor)</p> <p>G3 - high level of malignancy (undifferentiated tumor)</p>
P	Penetration	Depth of the tumorous infiltration into the walls of a hollow organ (histological criteria)	<p>P1- cancer infiltrating into the mucous membrane</p> <p>P2-cancer infiltrating into the submucosal layer</p> <p>P3-cancer infiltrating into as deep as the serous layer</p> <p>P4-cancer infiltrating into the serous layer or extending beyond the organ wall</p>

Treatment of the tumors. The malignant diseases call for immediate therapy, whereas benign masses require treatment if they

- cause disfunction of the organ affected;
- result in cosmetic defects;
- are found premalignant;
- are suspected of transforming into malignant ones.

The therapeutic methods for malignant disease include surgery, radiation, chemo- and/or hormone therapy. Surgery is the main method of treatment of malignant tumors and it is often combined with radiation or chemotherapy. This is referred to as combined therapy (for example,

in breast cancer, cancer of the uterus, ovaries, etc.). The radiation therapy can be either employed pre- or postoperatively. Surgery is not applied if the condition can be treated by radiation or drug therapy alone (e.g. cancer of the lip). When the tumor has advanced so far that successful surgery in view of a metastatic spread is very unlikely, the case is considered inoperable.

Operating on patients with malignant tumors, the surgeon should follow the principle of *ablasty*, which implies the prevention of spread of tumor cells during the surgery by means of removing the mass within the intact tissues. To avoid damaging the tumor, it is necessary to ligate the veins as early and excise the turnout, that tissues and lymph nodes en bloc.

The principle of *antiblasty* involves:

- 1) measures aimed at destroying the cancer cells in the operation site, in the wound, in the lymph vessels and veins using electrocautery, laser or plasmatic scalpels;
- 2) cleansing the wound after excision of the tumor with 70% alcohol solution;
- 3) regional infusions of chemotherapeutic drugs.

As the tumor cells can spread beyond the organ affected to the lymphatic vessels, lymph nodes and surrounding tissues, it is recommended that a large portion or the entire organ involved be removed together with the surrounding tissues and fasciae. This is known as the principle of zones. An operation for breast cancer serves as an illustration, in which case the breast with the fatty tissues, fasciae and the subclavial, axillary lymph nodes as well as the pectoralis major muscles are removed in bloc.

The radical operation involves the removal of the entire organ (e.g. the breast, uterus) or its large portion (the stomach, bowel) together with the regional lymph nodes. The *combined* surgery during which the organ affected is excised with part of or the entire organ into which the tumor has spread is also regarded radical. *Palliative* operations are performed to remove part or the entire organ if the metastases are not liable to ablation. They are indicated when complications of the malignancy are found (e.g. tumor decay with bleeding, perforation of gastric or colonic cancer). *Symptomatic* operations are aimed at eliminating complications caused by the enlarged tumor without removing the tumor itself (e.g. gastrostomy in esophageal cancer; inter intestinal anastomosis in bowel cancers complicated by intestinal obstruction, tracheostomy in cancer of the larynx).

Cytoreductive operation is the surgical removal of part of a malignant tumor which cannot be completely excised, so as to enhance the effectiveness of radiation or chemotherapy. It is used only in specific malignancies, as generally partial removal of a tumor is not considered a worthwhile intervention. Ovarian carcinoma and some types of brain tumor are reduced prior to commencing radio- or chemotherapy. It may also be used in the case of slow growth tumors to shift tumor cells from phase of cell cycle to replicative pool. It is usually a long and often complicated procedure taking several hours or more to perform, depending on internal involvement and location.

Radiation therapy. Above half of the patients with malignant tumors are exposed to radiotherapy. It can either be used as an independent method for early stages of the disease (e.g. cancer of the lower lip, cervix of the uterus and the skin) or is included in the combined therapy. Radiation therapy is commonly coupled with surgery and undertaken either pre- or postoperatively. In addition, radio-therapy can be combined with chemo- or hormone therapy. The curative effect on the tumor and its metastases is achieved through external, intra-cavitary or interstitial radiation. External radiation involves g-therapy with radioisotopes (^{60}Co , ^{137}Cs , etc.). In intra-cavitary radiation therapy the source of radiation is introduced into a natural cavity (e.g. the oral cavity or uterine cavity, urinary bladder, maxillary antrum etc.). To perform interstitial radiation, isotopes are inserted directly into the tissues using needles or capsules after the removal of the tumor (e.g. postmastectomy). Staying in the tissues for long periods the isotopes act on the residual tumor cells and their metastases, to the lymph nodes. Radiation therapy as well as chemotherapy can be adjuvant and neoadjuvant. Adjuvant therapy – is therapy given to destroy left-over (microscopic) cells that may be present after the known tumor is removed by surgery. Adjuvant therapy is given to prevent a possible cancer reoccurrence.

Neoadjuvant therapy - therapy given prior to the surgical procedure. Neoadjuvant therapy may be given to attempt to shrink the cancer so that the surgical procedure may not need to be as extensive.

Chemotherapy. The most common malignant tumors (e.g. cancers of the lung, breast, stomach and intestines) are known to respond poorly to drug therapy as compared to surgical and radiation therapy. Hence, the use of chemotherapy in combination with other methods of treatment.

The groups of chemotherapeutic agents:

1. Cytostatics (novembihin, cyclophosphan, TEPA, dopan, blastin, vincristin, etc.) hamper the growth of tumor cells, affecting cellular mitosis.
2. Antimetabolites alter the metabolism of cancer cells by
 - suppressing the synthesis of purins (mercaptopurin);
 - acting on the enzyme systems (fluoruracil, phthorafur) or on the transformation of folic acid (metotrexate).
3. Anti-cancer antibiotics are a group of compounds produced by fungi or microorganisms: actinomycin D, bruneomycin, mytomycin.
4. Monoclonal antibodies are a relatively new type of "targeted" cancer therapy. Antibodies are part of the immune system. Normally, the body creates antibodies in response to an antigen (such as a protein in a germ) entering the body. The antibodies attach to the antigen in order to mark the antigen for destruction by the body's immune system. In the laboratory, scientists analyze specific antigens on the surface of cancer cells (target) to determine a protein to match the antigen. Then, using protein from animals and humans, scientists work to create a special

antibody that will attach to the target antigen. An antibody will attach to a matching antigen like a key fits a lock. This technology allows treatment to target specific cells, causing less toxicity to healthy cells. Monoclonal antibody therapy can be done only for cancers in which antigens (and the respective antibodies) have been identified

Hormone therapy. Hormones are a treatment of choice for hormone receptor-positive tumors. These medications supplement are combined therapeutic methods of surgery, radiotherapy and chemotherapy. The preparations of the male sex hormone — androgen (testosterone propionate, methyl testosterone) are indicated in breast cancer, whereas those of female sex steroid - estradiol (synestrol and diethylstilboestrol) are known to be effective in cancer of the prostate. Hormone therapy of tumors also includes surgeries on the endocrine glands e.g. surgical or radiation castration of women with breast cancer.

The patient with malignancy may first report to a physician of whatever speciality, the oncological alertness is important for each health care professional. The oncological alertness implies:

1. Physician's knowledge of early and/or atypical symptoms and signs of malignancy and its complications.
2. Physician's knowledge of the clinical pictures of premalignant conditions and their treatment.
3. The timely referral of patients with supposedly malignant conditions to specialized medical centers.
4. The adequacy of the patient's examination by the physician who was the first to suspect the malignancy irrespective of their speciality.