# 10.4 Tumor growth and development

## 10.4.1 Tumor classification

Tumors (abnormal formation of tissue) are classified as **malignant** (cancer-producing) or **benign** (non-cancer producing).

Tumors are named according to the tissue from which they arise. **Carcinomas** are malignant tumors derived from epithelial tissue, **sarcomas** from connective tissue and **lymphomas** from lymphatic tissue. **Leukaemias** usually involve an abnormal proliferation of blood-forming cells, in which malignant cells are widely dispersed and infiltrate bone marrow and lymphatic tissue.

## 10.4.2 Malignant tumor growth

Malignant tumors arise as a result of **uncontrolled autonomous** proliferation of the cancer cells. A typical feature of malignant tumor growth is invasion of surrounding host tissue, which is accompanied by some cell surface changes of malignant cells. Tumor growth rates vary and are influenced by vascular supply, immune surveillance mechanisms, by occurence of non-proliferating cells, by proteolytic enzymes, growth factors etc.

Most tumors are considered to be monoclonal. However, during the course of tumor growth heterogenous mixture of cells can occur resulting from angiogenesis, cell differentiation etc. Some subpopulation of tumor cells may remain in non-reproductive stage ($G_0$ phase). These non-proliferating cells may be resistant to therapy.

## 10.4.3 Tumor angiogenesis

Tumor angiogenesis is **new growth of blood vessels to vascularize tumor by penetration of the capillaries from the edges of tumor**. Malignant cells produce tumor angiogenesis factor (TAF), promoting growth of the network of blood vessels in the tumor (Fig. 10.6). Also decreased $pO_2$ in central parts of tumor may play a role in angiogenesis. Tumor angiogenesis may be insufficient in tumors with rapid rate of growth. Later the tumor necrosis with releasing of necrotoxins may develop. A slowing down of tumor growth may result from the depletion of oxygen and nutrients.

## 10.4.4 Pathogenesis of metastasis

A typical characteristic of malignancy is metastasis. Metastasis is the **dissemination of clumps of cancer cells from a primary site of origin to a secondary site**. 50 % of newly diagnosed patients with malignant tumors have occult metastases that are not readily detectable.

Malignant cells disseminate by these routes

- through lymphatic vessels (invasion into small lymphatic vessels)
- through blood vessels (invasion into venules and capillaries)
- through serous surfaces of body cavities (implantation in the peritoneal, pleural space etc.)

The process of metastasis involves several steps:

1. local invasion of the surrounding tissue
2. penetration of tumor cells into blood vessels or lymphatics
3. transport in the blood or lymph circulation
4. arrest in capillary bed of organs
5. adherence to vascular wall
6. escape from vessels
7. proliferation of cells at the secondary site

Release of cancer cells from primary tumor can be associated with palpation, puncture and surgery and therefore manipulation of the tumor must be careful.

However, many millions of cancer cells may break off primary tumor and never set up metastases because of most die within lymphatics or bloodstream.

Metastatic cells may exhibit differences from cells of primary tumor. These differences may be associated with some tissue characteristic of secondary sites.

Metastases occur frequently in the liver, lungs (Fig. 10.7), brain, bones etc. Destruction of these

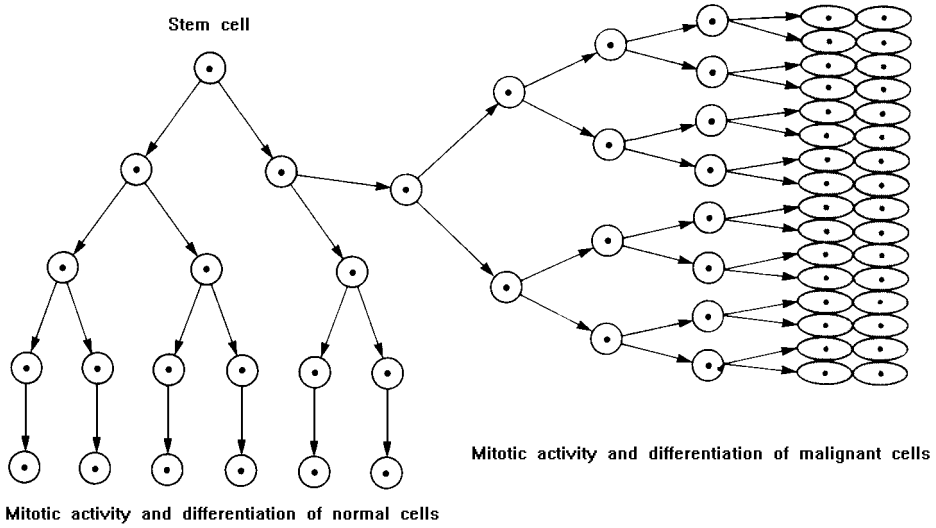


Figure 10.5: Mitotic activity and differentiation of normal and malignant cells (from Groer MW: Basic pathophysiology, 1989)

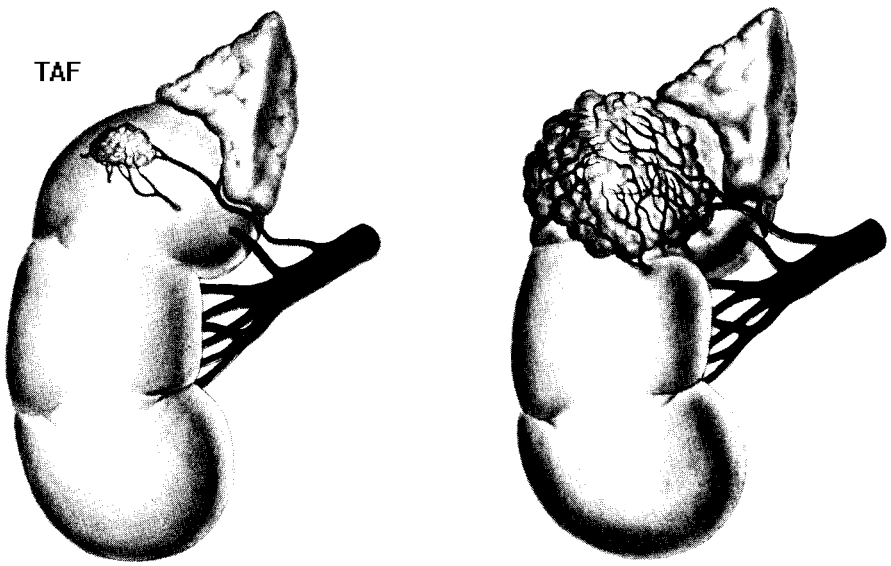


Figure 10.6: Tumor angiogenesis (adapted from McCance, Mooney KH, Roberts LK: Pathophysiology, 1990)

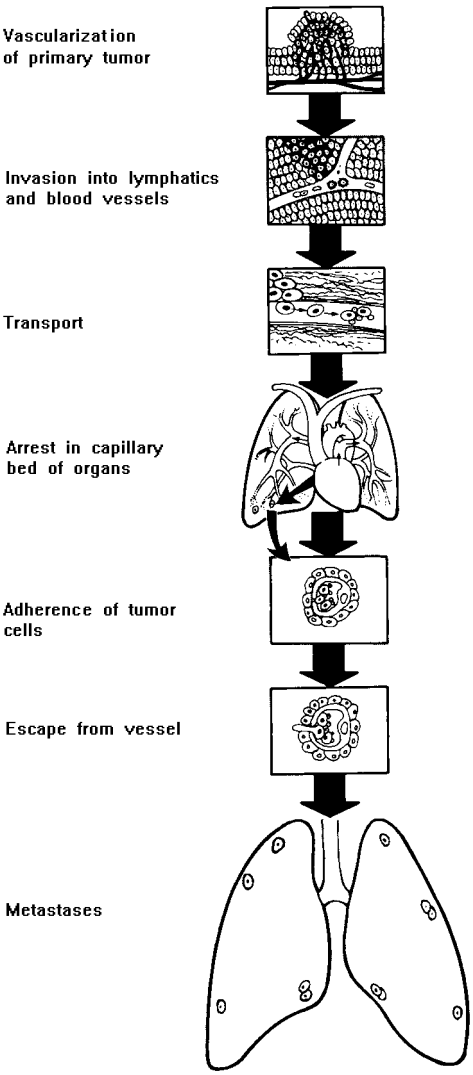


Figure 10.7: Pathogenesis of metastasis (from Poste & Fidler, 1980)

organs can often be found in cancer patients with metastases.

Some tumor types preffer certain sites of secondary growths (e.g. breast carcinoma and carcinoma of the prostate, kidney metastasize to bone, melanoma-skin cancer metastasizes to liver). The mechanical theory of metastasis explain the spread of cancer cells to certain organs to such factors as metastatic cell size, pressure, size of vessels, direction of bloodstream or lymphatic drainage etc. The selective affinity theory of metastasis correlates higher afinity of metastatic cells to certain enviroment with immunologic characteristics, local growth factors, specific glycoprotein surface components of favorable tissue cells etc.

## 10.5 Predisposing factors of cancer cells

Epithelial tissue sometimes shows such deviation from normal tissue growth as **hyperplasia, metaplasia and dysplasia**. These changes may predispose to cancer. They occur as dysplasia of cervix uteri, polyposis coli, chronic cystic mastitis etc.

**Carcinoma in situ** represents preinvasive epithelial tumor with atypical cell changes without disruption of basement membranes. Some preinvasive lesions may progress to invasive forms, some are unchanged and some may spontaneously regress.

## 10.6 Characteristics of benign tumors

Benign tumor is classified on the basis of **well differentiated cells, which do not invade and cannot set up a new growths – metastases**. Benign tumors are usually **separated** from the surrounding host tissue by a capsule of connective tissue. Benign tumor **growth is slow**. Necrosis and ulcerations of these tumors are unusual. However, benign tumor can represent sometimes extremely serious problem (if it obstructs a bronchus, vessel, truct, if it interferes with oxygenation, nutrition or elimination, if it has functional endocrinal activity etc.)