Figure 10.8: Factors contributing to cachexia in cancer patients

10.7   Pathophysiology of malignant disease

Systemic and organ-specific signs and symptoms of tumor growth and dissemination are included in malignant disease. **Grading** (degree of malignancy) and **staging** (stage of development of malignant disease) are helpful in diagnosis of malignant disease.

Tumors are graded by biopsy according structural features that reflect the degree of differentiation. There are four grades of malignancy from tumors which are well differentiated and have low degree of malignancy (grade I.) to very poorly differentiated tumors with no resemblance to tissue of origin, with high mitotic activity and great cellular variability with high degree of malignancy (grade IV.).

TNM system is international accepted classification of stage of malignant disease. Tumor progression is related to three components included in this classification (T–tumor, N–nodes, M–distant metastases).

Cancer patients have often suffered from cachexia, pain, infection, anaemia, ulceration, compression,
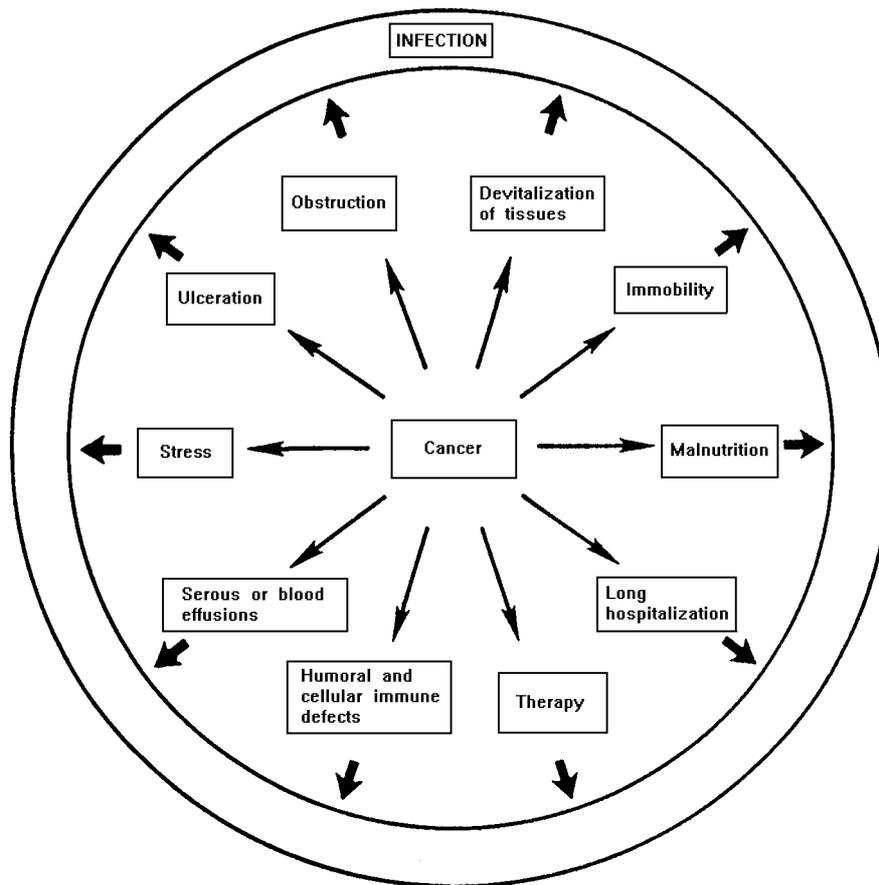
Figure 10.9: Factors predisposing to infection in cancer patients

obstruction, destruction of vital organs, skin and connective tissue abnormalities etc.

10.7.1 Cachexia

Cachexia is closely related to anorexia. Cachexia is manifested by weight loss, wasting, weakness, loss of mobility, fluid and electrolyte dysbalance, anaemia, malnutrition. Cachexia is observed in at least 2/3 of oncologic patients and may be the first symptom. Cachectic wasting is the most common cause of death particularly in patients with stomach, colon, rectum or breast cancer.

Anorexia can be due to pain, depression, altered taste sensations, aversion to certain foods (such as meat, chocolate etc.) Hyperglycaemia, hyperproteinaemia (results of abnormal metabolism) and specific anorexigenic polypeptides (produced by tumors) can act directly on hypothalamic satiety center. Cachexia may result from special competitive uptake of specific nutrients by malignant tumor that results in lack of nutrients in host. Several factors contributing to cachexia are shown on Fig. 10.8.

10.7.2 Infection

Infection is one of the most serious complication and common cause of death in cancer patients. Factors predisposing to infection are shown on Fig. 10.9. Common agents causing infection in cancer patients
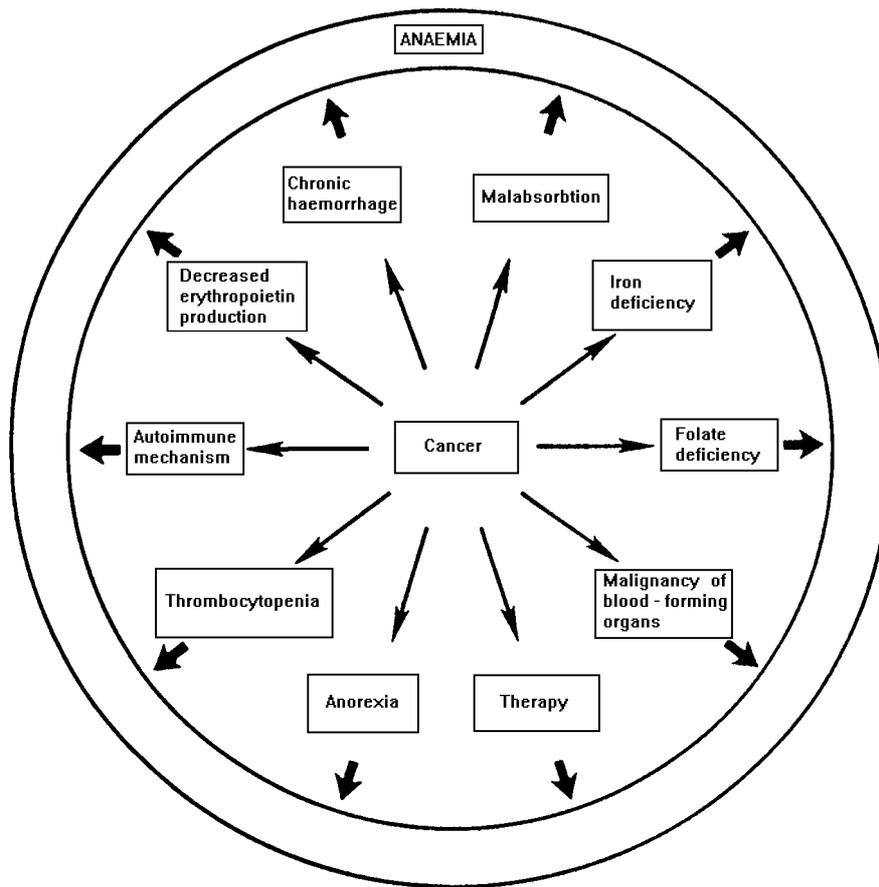
Figure 10.10: Factors associated wit anaemia in cancer patients

are E. coli, Pseudomonas, Klebsiella, Staphylococcus, Candida, Streptococcus, Proteus, Clostridium, viruses and protozoa.

10.7.3   Anaemia

Anaemia may develop in most of cancer patients. Approximately 20 % of all cancer patients have anaemia with Hgb lower than 9 g/dl. Factors causing anaemia in cancer patients are shown on Fig. 10.10.

10.7.4   Leukopenia and thrombocytopenia

Leukopenia and thrombocytopenia can be caused by

- direct tumor invasion and metastasis to bone marrow

- myelotoxic chemotherapy and radiotherapy

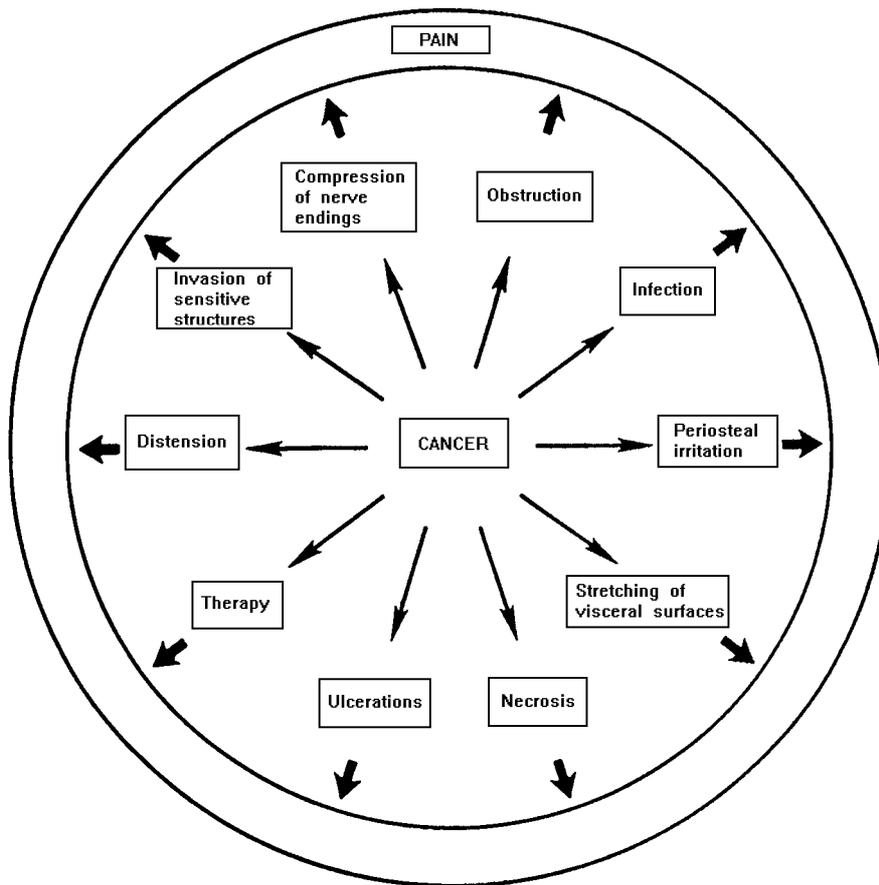- disseminated intravascular coagulation

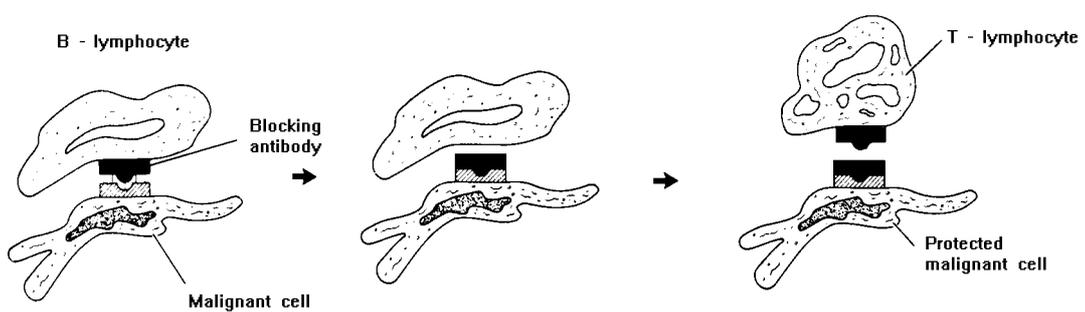Figure 10.11: Factors contributing to pain in cancer patients

Figure 10.12: Protection of malignant cell from immunologic surveillance. Antibodies produced by B lymphocytes block the cell from destruction by T lymphocytes. (From Groer MW, Basic Pathophysiology, 1989)

10.7.5   Pain

Pain is unusal symptom in the early stages of malignant disease, but pain does affect 60-80 % patients with advanced cancer. Pain may be enhanced by anxiety, sleep loss, fatigue etc. Mechanisms causing pain in cancer patients are shown on Fig. 10.11.

Serious complications induced by nephrotoxic, myelotoxic, cardiotoxic, neurotoxic chemoterapy and radiotherapy are also of considerable importance in oncologic patients.

10.8   Immune surveillance and cancer

Immune system plays an important role in **immunologic surveillance** for the emergence of cancer cells. A normal immunologic surveillance recognizes altered cell surface (specific and non-specific) tumor antigens and reacts against them. Up to 10 million malignant cells can be destroyed by immune system. (Tumor 1 cm in diameter contains approximately 10^9 cells after 30 doubling-times.)

A wide range of cell mediated and humoral immune responses can protect the host against cancer cells – cytotoxic T lymphocytes (Tc cells), natural killer (NK) cells, macrophages, helper T lymphocytes, B lymphocytes, cytotoxic antibodies and complement system.

However, cancer cells are capable to escape immunologic surveillance. Escape mechanisms include:

1. antigenic modulation (by capping with antibodies, masking by glycocalyx coat, shedding)

2. non-antigenic subclone of cells (which may arise during tumor progression)

3. suboptimal number of Tc cells (tumor grows at increased rate)

4. stimulation of supressor T lymphocytes (blocking immune response)

5. immunosupressive substance prostaglandin E is produced by some tumors (PgE acts by increasing c AMP levels in lymphocytes and thus blocks their proliferation)

6. B-lymphocytes may transfer antibodies blocking T lymphocyte receptors on malignant cells, therefore T lymphocytes cannot destroy these cancer cells (Fig. 10.12)

7. cachexia

8. immunosupressive therapy

There is an increased cancer risk in individuals with immunodeficiency (inherited or acquired). Such individuals have 14-fold increased risk of developing lymphomas, 4-21-fold increased risk of skin cancer, 11-fold increased risk of stomach cancer, 13-fold increased risk of uterine cervix cancer, 2-fold increased risk of urinary bladder cancer.

Of particular interest in cancer research and clinical practice are mind-body relationships studied in **psychoneuroimmunology**.

Stressors may supress the immune system through several mechanisms (release of catecholamines and corticosteroids, central mechanisms etc.). Immunosupression results in increased susceptibility to malignancy with negative influence on incidence and mortality from malignant disease.

However, ability to cope with stressors plays also an important role. Several studies demonstrated that "fighting" and denial patients are associated with longer survival than non-fighting and depressed patients.