

UNVEILING CANCER: AN IN-DEPTH EXPLORATION OF CAUSES, RISK FACTORS, PATHOPHYSIOLOGY, CLINICAL MANIFESTATIONS, AND TREATMENT OPTIONSMekala Anusha¹, Shaik Parveen², *Asfia Tabassum³ and Dodda Thanmai Naga Bhavani⁴^{1,2}Assistant Professor, Malla Reddy College of Pharmacy.^{3,4}Student, Malla Reddy College of Pharmacy.***Corresponding Author: Asfia Tabassum**

Student, Malla Reddy College of Pharmacy.

Article Received on 13/01/2025

Article Revised on 02/02/2025

Article Accepted on 23/02/2025

ABSTRACT

Cancer is a leading cause of death worldwide, accounting for millions of deaths annually. It is a complex and multifactorial disease characterized by uncontrolled cell growth, invasion, and metastasis. Risk factors for cancer include genetic predisposition, environmental factors, lifestyle choices, and infectious agents. Clinical presentation varies depending on the type and location of the cancer, but common symptoms include pain, weight loss, fatigue, and changes in skin or bowel habits. Early detection and treatment are critical to improving cancer outcomes and reducing mortality. Treatment options include surgery, chemotherapy, radiation therapy, and targeted therapies, which may be used alone or in combination. Despite advances in cancer treatment, there is still a need for more effective and less toxic therapies. Ongoing research is focused on developing new treatments and improving existing ones to enhance patient outcomes.

KEYWORDS: Cancer, Surgery, Chemotherapy, Radiation therapy, Prostate cancer, Breast cancer, Head and Neck cancer, Ovarian cancer, Lung cancer, Liver cancer.

INTRODUCTION**I. DEFINITION OF CANCER**

Cancer is a group of diseases characterized by the uncontrolled growth and spread of abnormal cells. It occurs when the normal mechanisms that control cell growth and division are disrupted, leading to the formation of malignant tumors.

Metastasis refers to the spread of cancer cells from the primary tumor to distant organs, playing a major role in cancer-related deaths. This complex process consists of several stages, including the invasion of nearby tissues, entry into the circulatory or lymphatic system, movement through the body, exit from the vessels, and formation of secondary tumors in new locations.

Compared to localized cancer, metastatic disease presents greater treatment challenges, often necessitating systemic approaches like chemotherapy, immunotherapy, or targeted therapy. Gaining deeper insights into the molecular pathways driving metastasis is essential for developing advanced therapeutic strategies and improving survival rates in affected patients.^[1-6]

II. STAGES OF CANCER

Cancer staging is commonly determined using the TNM system, which evaluates tumor size, lymph node

involvement, and metastasis. This classification divides cancer into five key stages.

- **Stage 0 (Carcinoma in Situ):** At this stage, abnormal cells are detected but remain confined to their original site without invading surrounding tissues. It is considered non-invasive and has a high likelihood of successful treatment.
- **Stage I (Early-Stage Cancer):** The cancer is still localized within the organ where it originated. The tumor remains small, and there is no evidence of lymph node involvement.
- **Stage II (Localized Cancer with Limited Spread):** The tumor has increased in size but is still contained within the primary organ. There may be minimal spread to nearby lymph nodes, but no distant metastasis has occurred.
- **Stage III (Regionally Advanced Cancer):** The cancer has grown significantly and has spread more extensively to nearby lymph nodes. However, it has not yet reached distant organs.
- **Stage IV (Metastatic Cancer):** At this most advanced stage, cancer has spread beyond the original organ to distant parts of the body. Treatment is typically systemic and focuses on disease management rather than cure.^[7]

III. TYPES OF CANCER

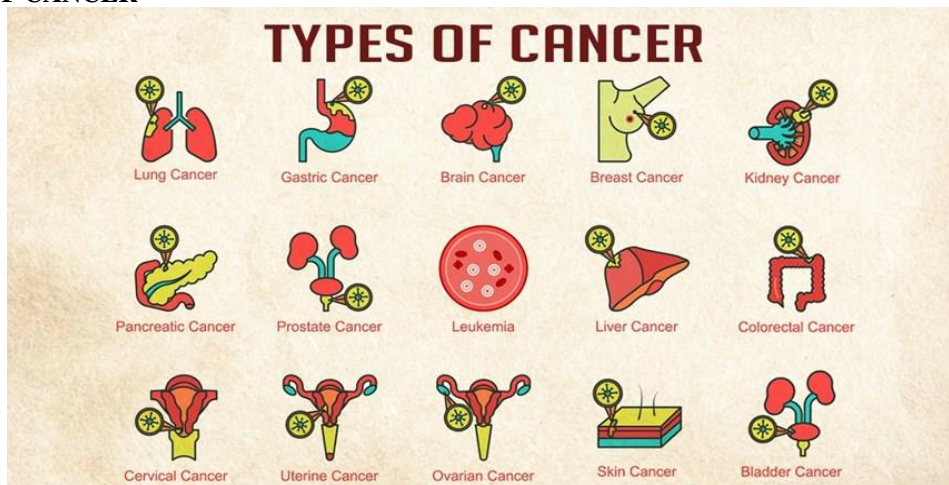


FIG. NO. 1: Types of Cancer.

Cancers can be broadly classified into several types based on their origin, behavior, and characteristics.

1. CARCINOMAS: Carcinomas are the most common type of cancer, accounting for about 85-90% of all cancers. They arise from epithelial cells, which form the lining of organs and glands. Examples of carcinomas include.

- Breast cancer
- Lung cancer
- Colorectal cancer
- Prostate cancer

SUB-TYPES OF CARCINOMA

Carcinomas are cancers that begin in the epithelial cells of the skin or internal organs. These cancers are classified based on the tissue type where they develop.

-The main subtypes are

1. Adenocarcinoma

Origin: Glandular Epithelium

Examples: Breast cancer, Lung Adenocarcinoma, Colon Adenocarcinoma.

2. Squamous Cell Carcinoma (SCC)

Origin: Squamous Epithelium

Examples: Skin cancer due to sun exposure, Lung SCC in smokers.

3. Basal Cell Carcinoma (BCC)

Origin : Basal layer of the Epidermis.

Examples : Slow-growing skin cancer often caused by UV exposure.

4. Transitional Cell Carcinoma

Origin: Transitional epithelium lining the Bladder and Urinary tract.

Examples: Bladder cancer.

5. Small Cell Carcinoma: Typically found in the lungs, this carcinoma grows and spreads quickly.

6. Non-Small Cell Lung Carcinoma (NSCLC): A group of lung cancer subtypes that includes adenocarcinoma, squamous cell carcinoma, and large cell carcinoma.^[1,2]

- **Characteristics of Carcinoma:** Carcinoma is a malignant tumor that originates from epithelial cells, which are found on the surfaces of organs, skin, mucous membranes, and glands. As the most prevalent form of cancer, carcinoma exhibits several key characteristics that distinguish it from other types of tumors.

Epithelial Cell Origin

Carcinomas arise from epithelial tissues that line the body's external and internal structures, including the skin, respiratory tract, digestive system, and glandular organs. These cells undergo genetic mutations and external influences that lead to uncontrolled proliferation and malignancy.

Unregulated Cell Growth and Structural Abnormalities

The development of carcinoma begins with dysplasia, a process where epithelial cells grow irregularly and lose their normal arrangement. Over time, if these changes progress unchecked, they can lead to invasive carcinoma, characterized by the ability of cancerous cells to penetrate the basement membrane and spread into deeper tissues.

Invasiveness and Metastatic Capability

A defining feature of carcinoma is its potential to invade nearby structures and spread to distant organs through the lymphatic system or bloodstream. This aggressive nature differentiates malignant carcinomas from benign growths, which remain localized.

Major Histological Subtypes

Carcinomas are categorized based on the type of epithelial cells they originate from and their structural characteristics. The most common subtypes include.

Squamous Cell Carcinoma (SCC)

Arises from squamous epithelial cells and frequently affects the skin, lungs, and esophagus.

Adenocarcinoma: Develops in glandular tissues and is often found in organs such as the breast, colon, prostate, and lungs.

Basal Cell Carcinoma (BCC): A slow-growing skin cancer that originates from basal keratinocytes, typically in sun-exposed areas.

Transitional Cell Carcinoma (TCC): Forms in the urinary tract lining, particularly the bladder.

Influence of Genetic and Environmental Factors

The emergence of carcinoma is driven by a combination of genetic mutations and environmental exposures. Chronic inflammation, viral infections (such as HPV in cervical cancer and *Helicobacter pylori* in gastric cancer), and harmful external factors like ultraviolet radiation and tobacco smoke contribute significantly to its development.^[8-15]

2. SARCOMAS: Sarcomas are cancers that arise from connective tissue cells, such as bone, cartilage, fat, and muscle. They are relatively rare, accounting for about 1% of all cancers. Examples of sarcomas include.

- Osteosarcoma (bone cancer)
- Soft tissue sarcoma
- Ewing's sarcoma

3. LEUKEMIAS: Leukemias are cancers that arise from blood cells, specifically white blood cells. They are characterized by the abnormal proliferation of immature white blood cells in the bone marrow. Examples of leukemias include.

- Acute myeloid leukemia (AML)
- Acute lymphoblastic leukemia (ALL)
- Chronic myeloid leukemia (CML)
- Chronic lymphocytic leukemia (CLL)

4. LYMPHOMAS: Lymphomas are cancers that arise from immune cells, specifically lymphocytes. They are characterized by the abnormal proliferation of lymphocytes in the lymphoid tissues, such as the lymph nodes, spleen, and bone marrow. Examples of lymphomas include.

- Hodgkin lymphoma
- Non-Hodgkin lymphoma

5. MELANOMAS: Melanomas are cancers that arise from pigment-producing cells, specifically melanocytes. They are characterized by the abnormal proliferation of melanocytes in the skin, leading to the formation of malignant tumors. Examples of melanomas include.

- Cutaneous melanoma
- Uveal melanoma

6. BRAIN AND SPINAL CORD TUMORS: Brain and spinal cord tumors are cancers that arise from the brain and spinal cord tissues. They can be benign or malignant, and are characterized by the abnormal proliferation of cells in the brain and spinal cord. Examples of brain and spinal cord tumors include.^[1,2]

- Glioblastoma
- Meningioma
- Medulloblastoma

IV. CANCER EPIDEMIOLOGY IN INDIA

India is experiencing a rising burden of cancer, with 14,61,427 new cases reported in 2022.

A. COMMON TYPES OF CANCER

1. Breast Cancer: Accounts for 14.8% of all cancer cases in females, with 2,21,757 new cases estimated in 2022.

2. Lung Cancer: Leading cause of cancer deaths in males, with 1,03,371 new cases estimated in 2022.

3. Cervical Cancer: Significant health concern in Indian women, with 1,23,907 new cases estimated in 2022.

4. Oral Cancer: Common type of cancer in India, particularly among males, with 1,98,438 new cases estimated in 2022.

B. REGIONAL VARIATIONS

1. North-East Region: Has a higher incidence of cancer, with a crude incidence rate of 135.4 per 100,000.

2. Urban-Rural Differences: Cancer incidence rates vary significantly between urban and rural areas, with higher rates reported in urban areas.

C. RECENT STATISTICS OF CANCER

Cancer remains one of the biggest global health challenges, with approximately 20 million new cases diagnosed worldwide in 2022, leading to 9.7 million deaths. According to estimates, the number of new cancer cases could reach 35 million annually by 2050.

In India, cancer incidence continues to rise. In 2022, there were around 1,461,427 new reported cases, with a crude incidence rate of 100.4 per 100,000 individuals. Among men, lung cancer was the most commonly diagnosed, while breast cancer remained the most prevalent among women.

This increasing trend is largely driven by factors such as population growth, aging, and lifestyle changes. Projections suggest that by 2025, cancer incidence in India could rise by 12.8% compared to 2020 (CancerFax, 2024). Healthcare experts highlight the significance of preventive measures, including a healthier diet, regular physical activity, and quitting smoking, in reducing cancer risks(16-25).

V. COMMON ETIOLOGY OF DIFFERENT CANCERS

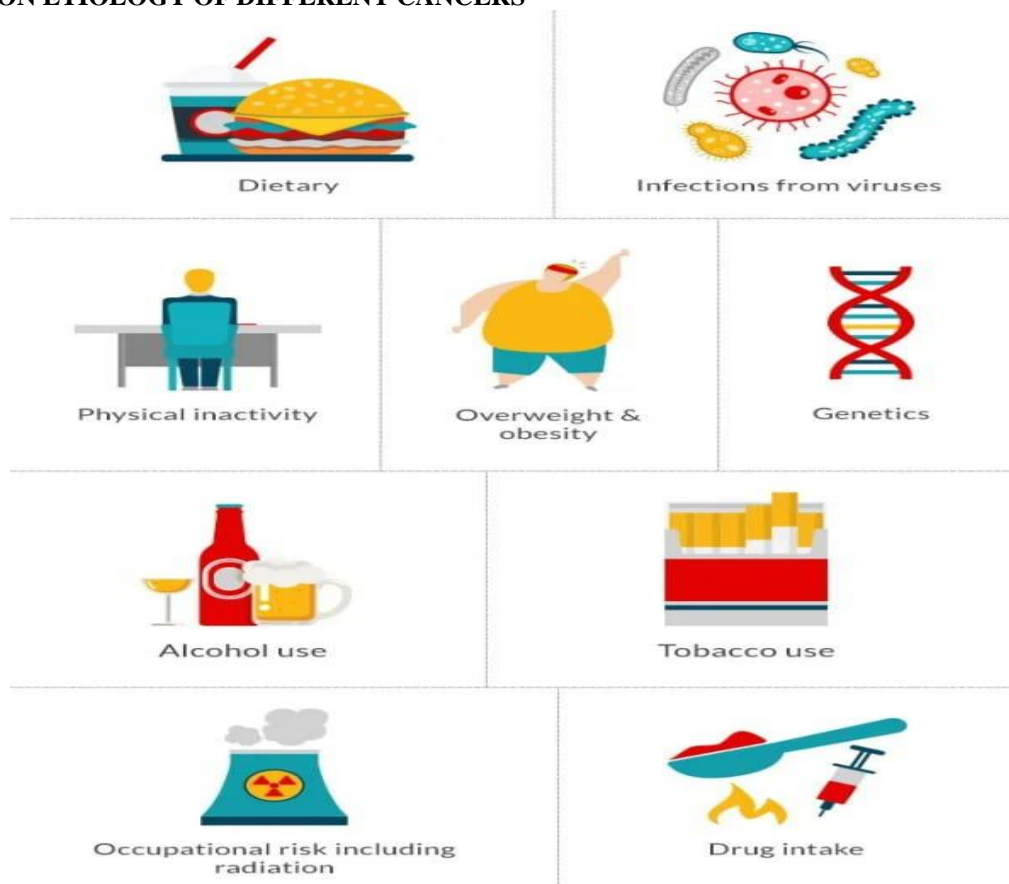


FIG. NO. 2: Etiology of Cancer.

Cancer can create due to a complex interaction of natural exposures, acquired characteristics, contaminations, and way of life habits.

A. NATURAL IMPACTS

- 1. Smoking:** Tobacco utilize is the first preventable cause of cancer and is unequivocally related with cancers such as lung and verbal cancers.
- 2. Bright (UV) Light:** Amplified introduction to UV rays—from the sun or tanning beds, compounded by ozone depletion—heightens the hazard of skin cancers.
- 3. Ionizing Radiation:** Presentation to ionizing radiation is connected to an expanded frequency of cancers like leukemia and thyroid cancer.
- 4. Discuss Quality:** Destitute discuss quality and contamination are related with a more prominent chance of respiratory cancers, counting lung cancer.

B. HEREDITARY INCLINATIONS

- 1. Family History:** A familial foundation of cancer can incline people to different cancers, counting breast, ovarian, and colon cancers.
- 2. Quality Transformations:** Particular changes, such as those in the BRCA1 and BRCA2 qualities, considerably hoist the hazard of breast and ovarian cancers.
- 3. Acquired Disorders:** Conditions like Li-Fraumeni disorder and Lynch disorder increment the probability of creating a few cancer types.

C. CONTAMINATIONS AS HAZARD COMPONENTS

- 1. HPV:** The human papillomavirus is a well-known cause of cervical cancer and other cancers in the anogenital locale.
- 2. Hepatitis B and C:** These viral contaminations altogether increment the hazard of liver cancer.
- 3. Helicobacter pylori:** Contamination with this bacterium has been connected to a higher rate of stomach cancer.

D. WAY OF LIFE CHOICES

- 1. Eat less:** Devouring a count calories tall in fats and moo in fiber is related with an lifted chance of cancers such as those of the breast and colon.
- 2. Physical Dormancy:** A inactive way of life can contribute to higher rates of colon and breast cancers.
- 3. Corpulence:** Overabundance body weight is recognized as a chance figure for a few sorts of cancer, counting those of the breast and colon.
- 4. Hormonal Variables:** The utilize of hormone substitution treatment has been associated to an expanded hazard of breast cancer.^[26-34]

VI. GENERAL CLINICAL PRESENTATION OF CANCER

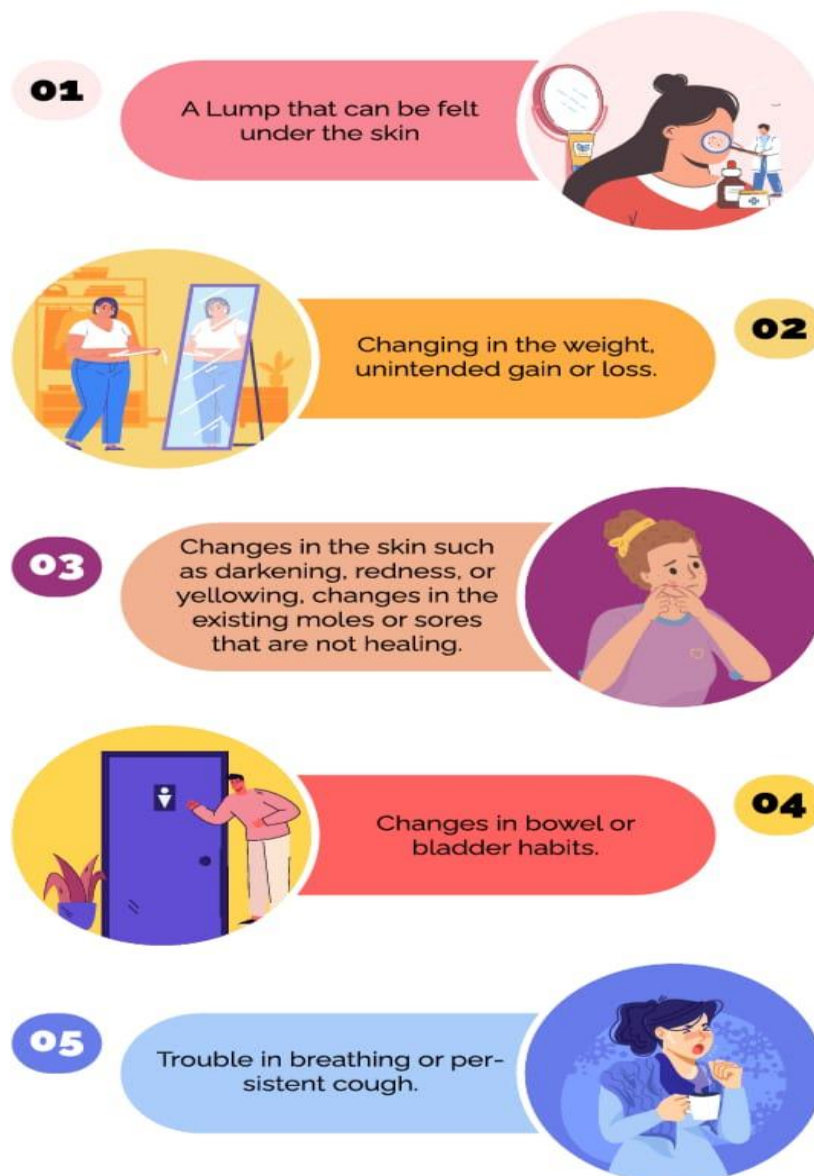


FIG. NO. 3: Signs & Symptoms of Cancer.

A. LOCAL SYMPTOMS

- 1. Pain:** A common symptom of various cancers, including bone, brain, and pancreatic cancer.
- 2. Mass or lump:** A palpable mass or lump can be a symptom of breast, thyroid, or testicular cancer.
- 3. Ulceration:** Skin cancers, such as basal cell carcinoma, can present with ulceration.
- 4. Bleeding:** Cancers of the lung, colon, or cervix can cause bleeding.

B. SYSTEMIC SYMPTOMS

- 1. Weight loss:** Unintentional weight loss is a common symptom of various cancers, including pancreatic, lung, and colon cancer.
- 2. Fatigue:** A general feeling of tiredness or weakness can be a symptom of various cancers, including leukemia, lymphoma, and colon cancer.

3. Fever: Some cancers, such as lymphoma or leukemia, can cause fever.

4. Sweating: Night sweats can be a symptom of lymphoma or leukemia.

C. PARANEOPLASTIC SYMPTOMS

1. Neurological symptoms: Some cancers, such as small cell lung cancer, can cause neurological symptoms, such as seizures or confusion.

2. Dermatological symptoms: Some cancers, such as breast cancer, can cause dermatological symptoms, such as skin rash or itching.

3. Endocrine symptoms: Some cancers, such as pancreatic cancer, can cause endocrine symptoms, such as diabetes or hypoglycaemia.^[35-41]

VII. THE COMMON PATHOPHYSIOLOGY OF VARIOUS KINDS OF CANCER

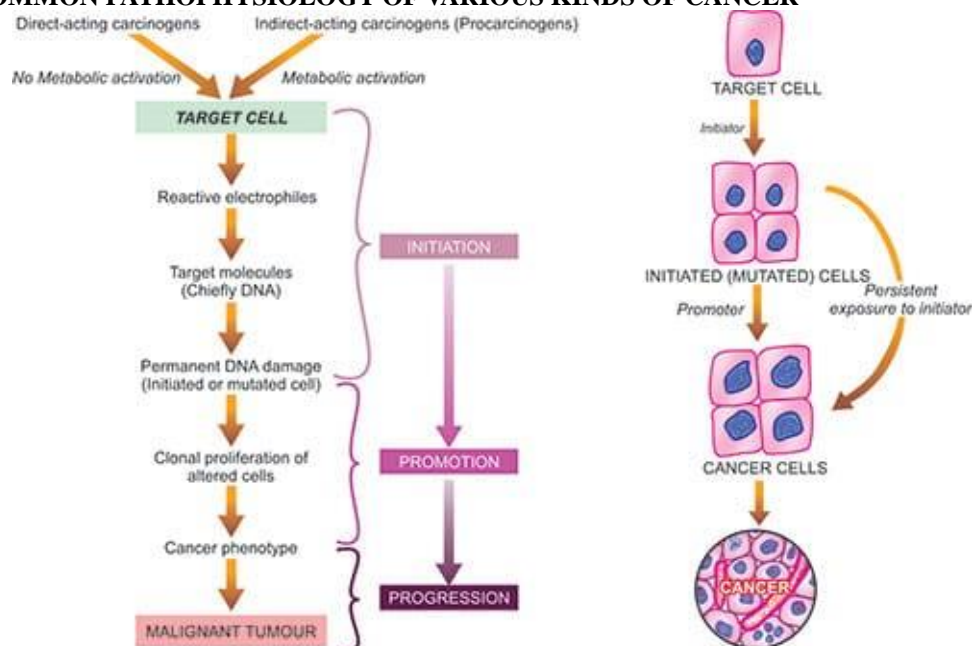


FIG.NO.4: Pathophysiology of Cancer.

A. GENETIC MUTATIONS

- 1. DNA damage:** Mutations in tumor suppressor genes or oncogenes can lead to uncontrolled cell growth.
- 2. Genetic instability:** Defects in DNA repair mechanisms can contribute to cancer development.

B. ABNORMAL CELL SIGNALING

- 1. Uncontrolled cell proliferation:** Activation of oncogenes or inactivation of tumor suppressor genes can lead to excessive cell growth.
- 2. Inhibition of apoptosis:** Cancer cells can evade programmed cell death, allowing them to continue growing uncontrollably.

C. TUMOR MICROENVIRONMENT

- 1. Angiogenesis:** Cancer cells can stimulate the formation of new blood vessels to supply themselves with oxygen and nutrients.
- 2. Immune evasion:** Cancer cells can evade the immune system by suppressing immune cell function or producing immune-inhibitory factors.

D. HORMONAL AND METABOLIC CHANGES

- 1. Hormone dysregulation:** Hormonal imbalances can contribute to cancer development and progression.

E. INFLAMMATION AND OXIDATIVE STRESS

- 1. Chronic inflammation:** Persistent inflammation can contribute to cancer development and progression (42-49).

VIII. MODIFIABLE AND NON-MODIFIABLE RISK FACTORS

Cancer development is influenced by a complex interplay of factors, some of which we can control

(modifiable) and others that we cannot (non-modifiable). Recognizing these factors is crucial for both prevention and early detection.

1. MODIFIABLE RISK FACTORS

Taking control: Many lifestyle and environmental factors contribute to cancer risk, and fortunately, these are often within our control.

A. Tobacco Use: Smoking or chewing tobacco significantly elevates the risk of numerous cancers, particularly lung, oral, and esophageal cancers. Eliminating tobacco use is one of the most impactful steps one can take for cancer prevention.

B. Physical Inactivity: A sedentary lifestyle increases the risk of several cancers, including colon and breast cancer. Regular physical activity is a key component of a cancer-preventive lifestyle.

C. Unhealthy Diet: Diets high in processed meats, sugar, and unhealthy fats are linked to increased cancer risk, particularly for colon and breast cancers. A balanced diet rich in fruits, vegetables, and whole grains is recommended.

D. Excessive Alcohol Consumption: Heavy alcohol use increases the risk of liver, breast, and other cancers. Moderation or abstinence is crucial.

E. Obesity: Being overweight or obese significantly raises the risk of various cancers, including breast and colon cancers. Maintaining a healthy weight through diet and exercise is essential.

F. Infections: Certain infections, such as human papillomavirus (HPV), hepatitis B and C, and *Helicobacter pylori*, are associated with increased risk for specific cancers. Vaccinations and appropriate treatment for these infections can reduce risk.

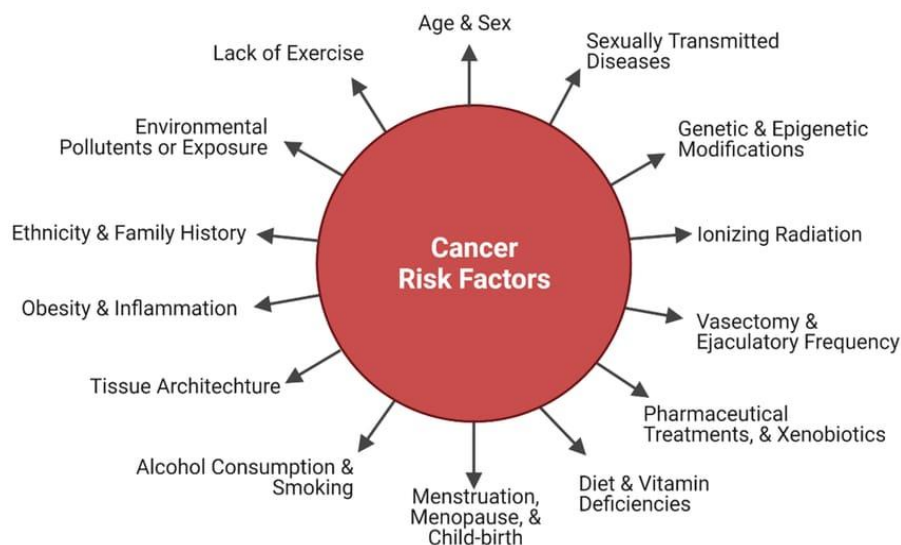


FIG. NO. 5: Risk Factors of Cancer.

2. NON-MODIFIABLE RISK FACTORS

Understanding Your Predispositions

While we cannot change these factors, understanding them is still important for awareness and early detection:

A. Age: Cancer risk increases with age, with the majority of diagnoses occurring in individuals over 65. Regular screenings become increasingly important as we age.

B. Family History: A family history of cancer can increase an individual's risk. Discussing family history with a doctor can help determine appropriate screening schedules.

C. Genetic Mutations: Inherited genetic mutations, such as BRCA1 and BRCA2, significantly increase the risk of certain cancers like breast and ovarian cancer. Genetic testing may be considered in some cases.

D. Radiation Exposure: Exposure to ionizing radiation, from sources like X-rays or nuclear accidents, increases cancer risk. Limiting unnecessary radiation exposure is important.

E. Environmental Factors: Exposure to certain environmental toxins, such as asbestos and benzene, is linked to increased cancer risk. Awareness of potential exposures and protective measures are crucial.^[50-55]

IX. DIAGNOSTIC CRITERIA FOR VARIOUS TYPES OF CANCER

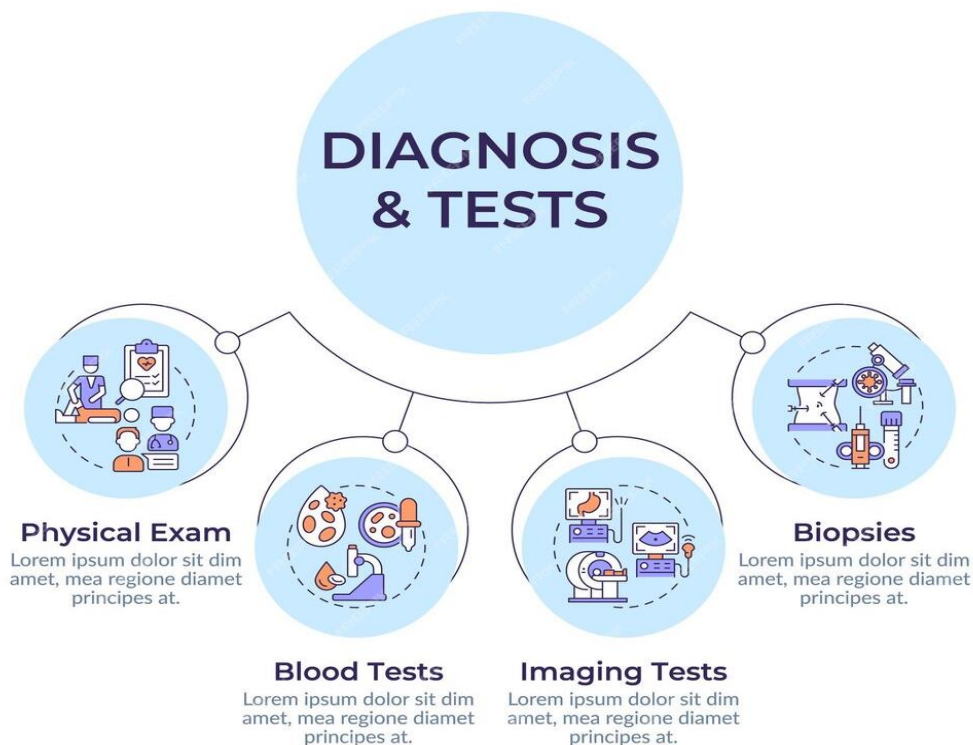


FIG.NO.6: Diagnostic Criteria for Cancer.

1. Breast Cancer

Breast cancer diagnosis primarily relies on imaging techniques such as mammography, ultrasound, and magnetic resonance imaging (MRI). Biopsies, including fine-needle aspiration, core needle biopsy, or surgical biopsy, confirm the diagnosis. Testing for biomarkers like HER2, estrogen receptor (ER), and progesterone receptor (PR) status is essential for treatment planning.

2. Lung Cancer

The diagnosis of lung cancer typically starts with imaging studies such as chest X-rays and computed tomography (CT) scans. Tissue samples are obtained through bronchoscopy, needle biopsy, or thoracentesis. Positron emission tomography (PET) is used to identify metastases, while genetic testing for EGFR and ALK mutations supports targeted therapy decisions.

3. Colorectal Cancer

Colorectal cancer is commonly diagnosed through fecal occult blood tests (FOBT) and colonoscopy, which allows for visualization and biopsy of suspicious areas. Additional diagnostic tools include CT colonography and genetic testing for conditions such as Lynch syndrome.

4. Prostate Cancer

Prostate cancer diagnosis involves prostate-specific antigen (PSA) testing and a digital rectal examination (DRE). Abnormal findings are confirmed through transrectal ultrasound-guided biopsy. Magnetic resonance imaging (MRI) may be utilized to assess the extent of the disease.

5. Leukemia

Leukemia is diagnosed through a complete blood count (CBC), peripheral blood smear, and bone marrow biopsy. Cytogenetic and molecular tests, such as fluorescence in situ hybridization (FISH) and polymerase chain reaction (PCR), help identify chromosomal abnormalities.

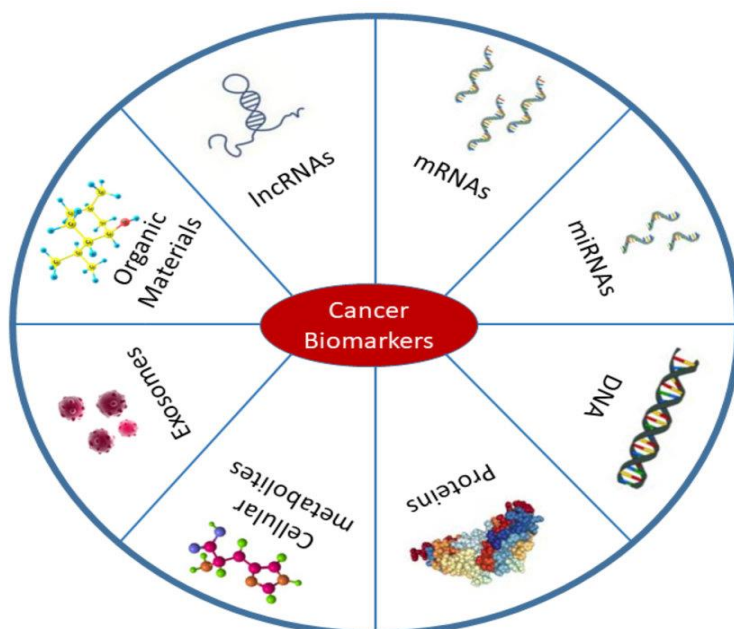
Tumor biomarkers are substances, including proteins, genes, or other molecules, that are produced by cancer cells or by the body in response to cancer. These biomarkers are essential tools in cancer care, aiding in diagnosis, prognosis, therapy selection, and monitoring for recurrence or progression.^[56-60]

X. BIOMARKERS

A. TYPES OF TUMOR BIOMARKERS

Tumor biomarkers are classified based on their clinical role.

- 1. DIAGNOSTIC BIOMARKERS:** Identify the presence of cancer (e.g., PSA for prostate cancer).
- 2. PROGNOSTIC BIOMARKERS:** Provide insight into the likely progression and outcome of the disease (e.g., HER2 in breast cancer).
- 3. PREDICTIVE BIOMARKERS:** Indicate the potential effectiveness of a particular treatment (e.g., EGFR mutations in lung cancer for targeted therapies).
- 4. MONITORING BIOMARKERS:** Track disease activity and detect recurrence after treatment (e.g., CEA for colorectal cancer).



FIGNO 7: Cancer Biomarkers.

B. EXAMPLES OF COMMON BIOMARKERS

1. PROSTATE-SPECIFIC ANTIGEN [PSA]: Used for prostate cancer screening and monitoring disease progression.

2. CANCER ANTIGEN 125 [CA-125]: Primarily used for diagnosing and monitoring ovarian cancer.

3. HUMAN EPIDERMAL GROWTH FACTOR RECEPTOR 2 [HER2]: Overexpressed in some breast cancers and used to guide targeted treatment decisions.

4. ALPHA-FETOPROTEIN [AFP]: Associated with liver cancer and certain types of germ cell tumors.

5. CARCINOEMBRYONIC ANTIGEN [CEA]: Commonly used in colorectal cancer to monitor recurrence or response to treatment.

C. APPLICATIONS IN CLINICAL PRACTICE

1. EARLY DETECTION: Biomarkers like PSA assist in identifying cancer at earlier stages, improving treatment outcomes.

2. DIAGNOSIS: Tumor markers support cancer diagnosis when other diagnostic tools, such as imaging or biopsy, are inconclusive.

3. PROGNOSIS: Biomarkers such as Ki-67 provide insights into tumor aggressiveness and disease progression.

4. TREATMENT GUIDANCE: Predictive markers like PD-L1 levels help identify patients who are likely to benefit from immunotherapy.

5. MONITORING: Biomarkers are essential for evaluating treatment responses and detecting potential relapses over time.

D. LIMITATIONS OF TUMOR BIOMARKERS

1. LACK OF SPECIFICITY: Some biomarkers may be elevated due to non-cancerous conditions, leading to false positives.

2. SENSITIVITY CHALLENGES: Not all cancers produce detectable levels of biomarkers, particularly in early stages.

3. FINANCIAL BARRIERS: Routine biomarker testing can be costly, limiting access for some patients.^[61]

XI. ADVERSE DRUG EFFECTS

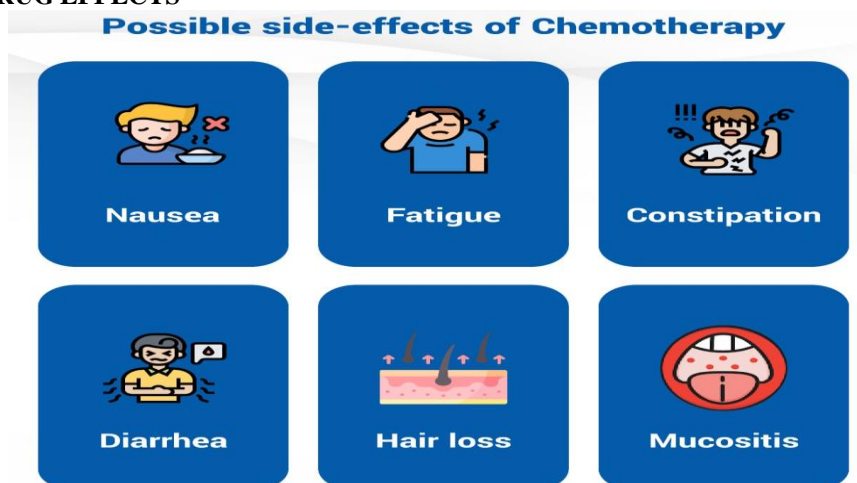


FIG. NO. 8: Side Effects of Chemotherapy.

I. CHEMOTHERAPY

1. Nausea and vomiting: Chemotherapy can cause stomach upset, leading to nausea and vomiting.

2. Fatigue: Chemotherapy can cause fatigue, which can range from mild to severe.

3. Hair loss: Many chemotherapy drugs cause hair loss, which can be temporary or permanent.

4. Mouth sores: Chemotherapy can cause mouth sores, which can be painful and make eating and drinking difficult.

5. Diarrhea or constipation: Chemotherapy can cause changes in bowel movements, leading to diarrhea or constipation.

6. Neutropenia: Chemotherapy can cause a decrease in white blood cells, making patients more susceptible to infection.

7. Anemia: Chemotherapy can cause a decrease in red blood cells, leading to anemia.

II. RADIATION THERAPY

1. Fatigue: Radiation therapy can cause fatigue, which can range from mild to severe.

2. Skin changes: Radiation therapy can cause skin changes, such as redness, itching, and blistering.

3. Hair loss: Radiation therapy can cause hair loss in the treated area.

4. Nausea and vomiting: Radiation therapy can cause nausea and vomiting, especially when treating the abdomen or pelvis.

5. Diarrhea or constipation: Radiation therapy can cause changes in bowel movements, leading to diarrhea or constipation.

6. Urinary frequency or burning: Radiation therapy can cause urinary frequency or burning, especially when treating the pelvis.

7. Infertility: Radiation therapy can cause infertility in both men and women.

III. HORMONE THERAPY

1. Hot flashes: Hormone therapy can cause hot flashes, which can range from mild to severe.

2. Night sweats: Hormone therapy can cause night sweats, which can disrupt sleep.

3. Vaginal dryness: Hormone therapy can cause vaginal dryness, which can lead to painful sex.

4. Mood changes: Hormone therapy can cause mood changes, such as depression or anxiety.

5. Weight gain: Hormone therapy can cause weight gain, which can increase the risk of other health problems.

6. Osteoporosis: Hormone therapy can cause osteoporosis, which can increase the risk of fractures.

7. Infertility: Hormone therapy can cause infertility in both men and women.

IV. IMMUNOTHERAPY

1. Fatigue: Immunotherapy can cause fatigue, which can range from mild to severe.

2. Rash: Immunotherapy can cause a rash, which can range from mild to severe.

3. Itching: Immunotherapy can cause itching, which can range from mild to severe.

4. Diarrhea or constipation: Immunotherapy can cause changes in bowel movements, leading to diarrhea or constipation.

5. Nausea and vomiting: Immunotherapy can cause nausea and vomiting, especially when treating the abdomen or pelvis.

6. Headache: Immunotherapy can cause headaches, which can range from mild to severe.

7. Infusion reactions: Immunotherapy can cause infusion reactions, which can range from mild to severe.

V. SURGERY

1. Pain: Surgery can cause pain, which can range from mild to severe.

2. Fatigue: Surgery can cause fatigue, which can range from mild to severe.

3. Nausea and vomiting: Surgery can cause nausea and vomiting, especially when treating the abdomen or pelvis.

4. Constipation: Surgery can cause constipation, which can range from mild to severe.

5. Urinary retention: Surgery can cause urinary retention, which can range from mild to severe.

6. Infection: Surgery can cause infection, which can range from mild to severe.

7. Scarring: Surgery can cause scarring, which can range from mild to severe.^[62-66]

XII. COMPREHENSIVE TREATMENT APPROACHES FOR DIFFERENT TYPES OF CANCER

A. TREATMENT OF PROSTATE CANCER

Prostate cancer is a common type of cancer that develops in the prostate gland, a small organ located below the bladder and in front of the rectum. The prostate plays an important role in producing seminal fluid, which supports and transports sperm.

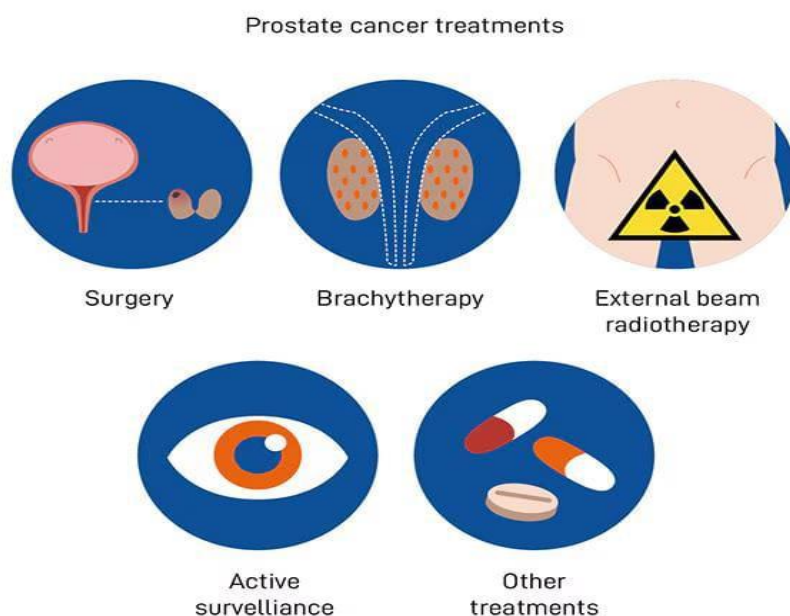


FIG. NO. 9: Treatments for Prostate Cancer.

PHARMACOLOGICAL APPROACHES

1. Active Surveillance: Regular monitoring without immediate intervention, suitable for low-risk cases.

2. Radiation Therapy: Includes external beam radiation therapy (EBRT) and brachytherapy for localized cancer.

3. Surgery (Radical Prostatectomy): Removal of the prostate gland, often performed for localized cancer.

4. High-Intensity Focused Ultrasound (HIFU): A minimally invasive therapy using focused ultrasound waves to destroy cancer cells.

5. Cryotherapy: Freezing and destroying prostate cancer cells, used for localized or recurrent cases.^[67]

6. Chemotherapy: Chemotherapy plays a crucial role in treating metastatic castration-resistant prostate cancer (mCRPC), particularly when hormonal therapies are no longer effective. The key chemotherapy drugs include:

- **Docetaxel (Taxotere):** Considered the first-line chemotherapy option for mCRPC, this drug is commonly administered alongside prednisone to enhance survival rates and manage symptoms.
- **Cabazitaxel (Jevtana):** Typically prescribed when the cancer continues to progress despite docetaxel treatment, cabazitaxel is also paired with prednisone for better efficacy.

- **Mitoxantrone:** Although used less frequently, this drug primarily alleviates symptoms rather than significantly extending survival.

- **Other Chemotherapy Agents:** In certain aggressive prostate cancer cases, carboplatin, cisplatin, and etoposide may be incorporated into treatment plans.^[68-71]

NON-PHARMACOLOGICAL APPROACHES

1. Lifestyle modifications: Includes dietary changes.

2. Exercise: Regular physical activity to improve overall health and potentially slow disease progression.

3. Psychosocial Support: Counseling or support groups to address mental health, stress, and emotional well-being.

4. Pelvic Floor Physiotherapy: Exercises to manage urinary incontinence following prostate cancer treatment.^[67]

B. TREATMENT OF LUNG CANCER

Lung cancer remains a leading cause of cancer-related deaths globally, with its treatment involving both pharmacological and non-pharmacological strategies.

-The choice of treatment depends on the type of lung cancer, its stage, and the patient's overall health.

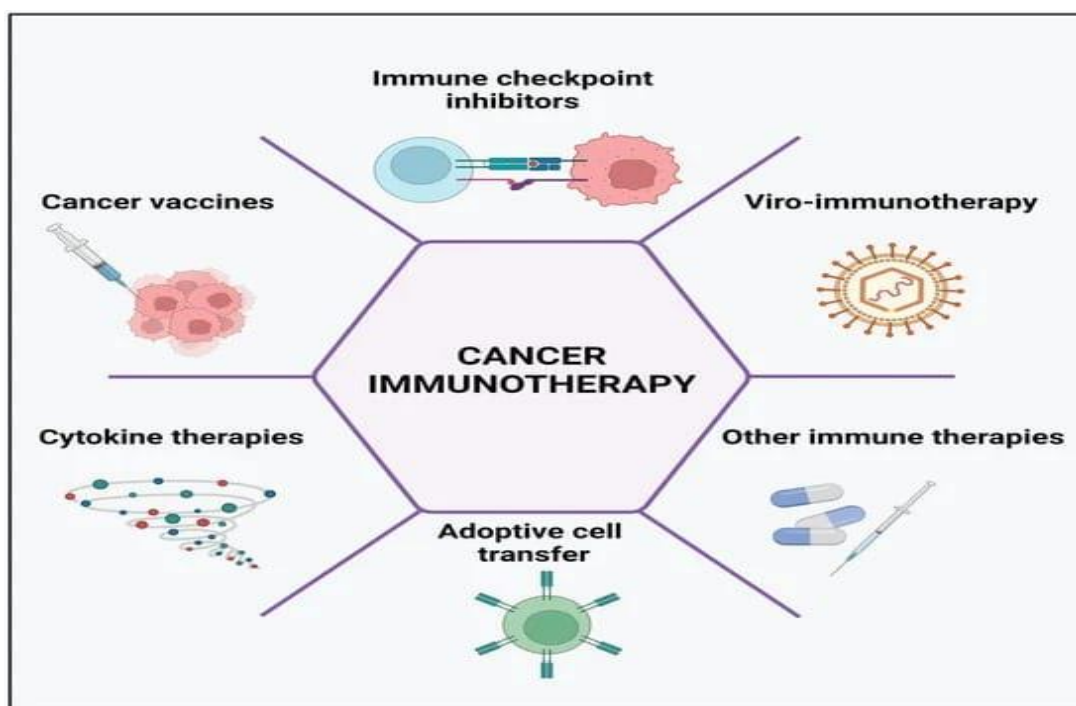


FIG.NO.10: Immunotherapy for Cancer.

PHARMACOLOGICAL APPROACHES

1. Chemotherapy

Chemotherapy plays a vital role in managing small-cell lung cancer (SCLC) and advanced non-small-cell lung cancer (NSCLC).

-Commonly used drugs include cisplatin or carboplatin, often combined with other agents such as etoposide or pemetrexed.

2. Immunotherapy

particularly immune checkpoint inhibitors like pembrolizumab and nivolumab, has transformed the treatment of advanced NSCLC by targeting the PD-1/PD-L1 pathway.

3. Targeted Therapy

For NSCLC patients with specific genetic mutations, targeted therapies such as EGFR inhibitors (e.g.,

erlotinib) or ALK inhibitors (e.g., crizotinib) are highly effective.

4. Radiotherapy Enhancers

Radiosensitizing agents are sometimes used to improve the effectiveness of radiation therapy, particularly in localized lung cancer.

NON-PHARMACOLOGICAL APPROACHES

1. Surgery

Surgical intervention, such as lobectomy or pneumonectomy, is the primary treatment for early-stage NSCLC. Surgery is often complemented by adjuvant therapies to improve outcomes.

2. Radiotherapy

Radiation therapy is a critical component in treating both SCLC and NSCLC, especially for patients who are not candidates for surgery. Advanced techniques like stereotactic body radiotherapy (SBRT) offer precise targeting, enhancing effectiveness while minimizing side effects.

3. Palliative Care

Non-pharmacological measures, including pulmonary rehabilitation, oxygen therapy, and counseling, are crucial for improving the quality of life in patients with advanced-stage lung cancer.

4. Lifestyle Interventions and Support

Smoking cessation is essential to halt disease progression. Nutritional support and psychological counseling are integral to holistic care.^[72-77]

C. TREATMENT OF OVARIAN CANCER

Ovarian cancer is a cancer that begins in the ovaries, which are part of the female reproductive system responsible for producing eggs and hormones like estrogen and progesterone. It is one of the most common gynecological cancers and is often diagnosed at a late stage due to the difficulty of early detection.

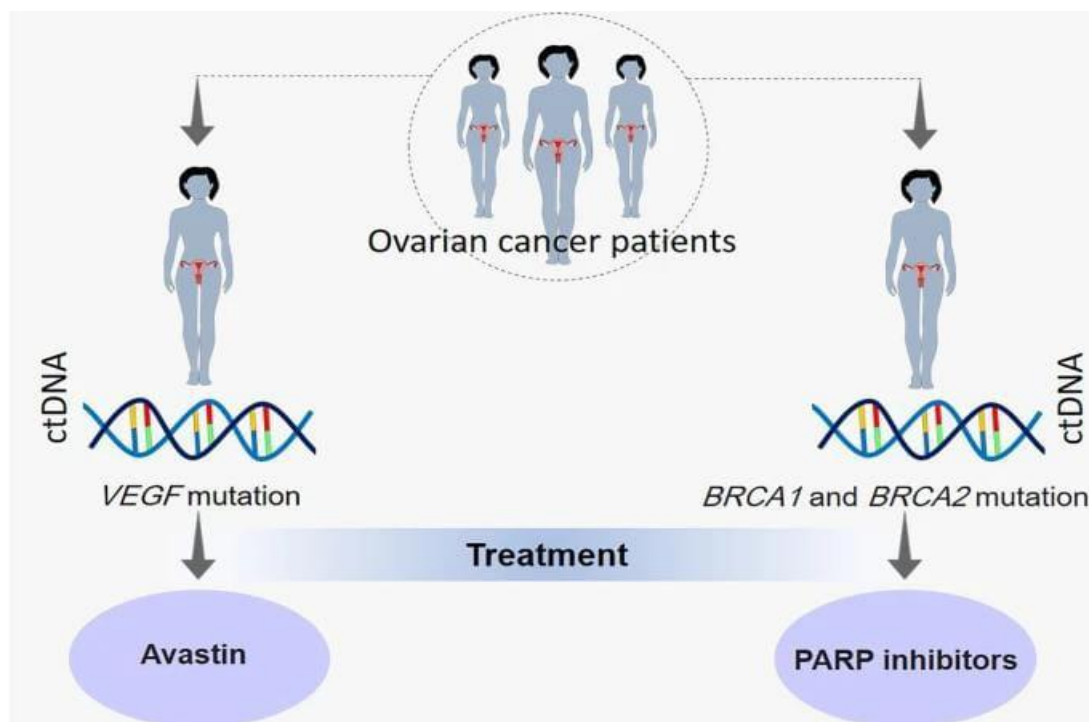


FIG. NO. 11: Treatment for Ovarian Cancer.

PHARMACOLOGICAL APPROACHES

1. Chemotherapy

Chemotherapy is a standard treatment for ovarian cancer, often administered after surgery to remove any remaining cancer cells. The combination of carboplatin and paclitaxel is commonly used to improve treatment outcomes.

2. Targeted Therapy

Targeted therapies are designed to target specific molecules involved in tumor growth. Bevacizumab, a monoclonal antibody targeting VEGF, is commonly used to block blood supply to tumors, hindering their growth.

3. Hormonal Therapy

Hormonal treatments, such as progestins, can be used in cases of hormone-sensitive ovarian cancer. However, they are typically less effective than chemotherapy or targeted therapies.

4. Immunotherapy

Immunotherapy, including immune checkpoint inhibitors like pembrolizumab, is being investigated for recurrent ovarian cancer. These drugs block the PD-1/PD-L1 pathway, helping the immune system target and destroy cancer cells.

NON-PHARMACOLOGICAL APPROACHES

1. Surgery

Surgery plays a critical role in treating ovarian cancer, especially through debulking, which involves removing as much tumor tissue as possible. Common surgical procedures include total hysterectomy, bilateral salpingo-oophorectomy, and omentectomy.

2. Radiation Therapy

While radiation therapy is not frequently used for ovarian cancer, it may be applied in some cases of recurrent or localized disease to reduce tumor size or alleviate symptoms.

3. Psychosocial Support

Providing psychological support is essential for ovarian cancer patients, as the disease can take a significant emotional and physical toll. Support groups, counseling, and mindfulness-based therapies can greatly enhance a patient's quality of life.

4. Nutritional Support

Proper nutrition is vital to maintain strength and overall health during cancer treatment. Specific dietary recommendations may be given to manage side effects such as nausea and weight loss.^[78-85]

D. TREATMENT OF HEAD AND NECK CANCER

Head and neck cancer (HNC) encompasses various malignant tumors located in areas such as the oral cavity, pharynx, larynx, and paranasal sinuses. The management of HNC typically involves a combination of pharmacological and non-pharmacological treatments, aimed at targeting the tumor, managing symptoms, and improving patient outcomes.

PHARMACOLOGICAL TREATMENT

1. Chemotherapy

Chemotherapy is often employed for advanced-stage cancers or in combination with other modalities like radiation. Key chemotherapeutic agents include.

Cisplatin: A platinum-based chemotherapy used frequently with radiation for advanced stages of HNC.

5-Fluorouracil (5-FU): A chemotherapy drug that inhibits cancer cell division.

Taxanes (e.g., Paclitaxel): These are used in combination therapies for more aggressive cancers.

2. Targeted Therapy

Drugs like Cetuximab, which target the epidermal growth factor receptor (EGFR), are used for specific types of HNC, particularly in patients who may not be suitable candidates for chemotherapy.

3. Immunotherapy

Recent advancements have introduced immunotherapy as an effective treatment option for recurrent or metastatic

HNC. Medications such as Nivolumab and Pembrolizumab, which block the PD-1 receptor, have shown promise in improving patient outcomes for these advanced stages.

NON-PHARMACOLOGICAL TREATMENT

1. Surgical Treatment

Surgery is often the primary treatment for localized head and neck cancers. The objective is to surgically remove the tumor and surrounding affected tissues, which may involve parts of the tongue, jaw, or larynx. Post-surgical reconstruction is frequently necessary to restore the function and appearance of the affected area.

2. Radiotherapy

Radiation therapy is a crucial component of treatment, typically used after surgery or in cases where surgery is not viable. It helps reduce tumor size, prevent recurrence, and manage inoperable cancers. Techniques such as intensity-modulated radiation therapy (IMRT) allow for precise tumor targeting while minimizing damage to healthy tissue.

3. Supportive Care

Supportive care plays a significant role in managing the side effects of cancer treatments and improving patients' quality of life. Important aspects of supportive care include.

4. Nutritional support: Patients often experience difficulties with eating and swallowing, making nutritional support vital during treatment.

5. Speech therapy

For patients who undergo surgery or radiation affecting speech and swallowing, speech therapy aids in recovery and rehabilitation.^[86-90]

E. TREATMENT OF BREAST CANCER

Breast cancer is a condition where abnormal cells in the breast multiply uncontrollably, resulting in a tumor. It can arise in various parts of the breast, such as the milk ducts (ductal carcinoma), lobules (lobular carcinoma), or, less commonly, other tissues.

It is one of the most frequently diagnosed cancers in women worldwide, though men can also develop it. Early detection through self-examinations, mammograms, and routine screenings plays a key role in successful treatment. Risk factors include genetic factors, hormonal changes, lifestyle habits, and environmental influences. Treatment options depend on the stage and type of cancer and may include surgery, radiation therapy, chemotherapy, hormone therapy, or targeted therapies.

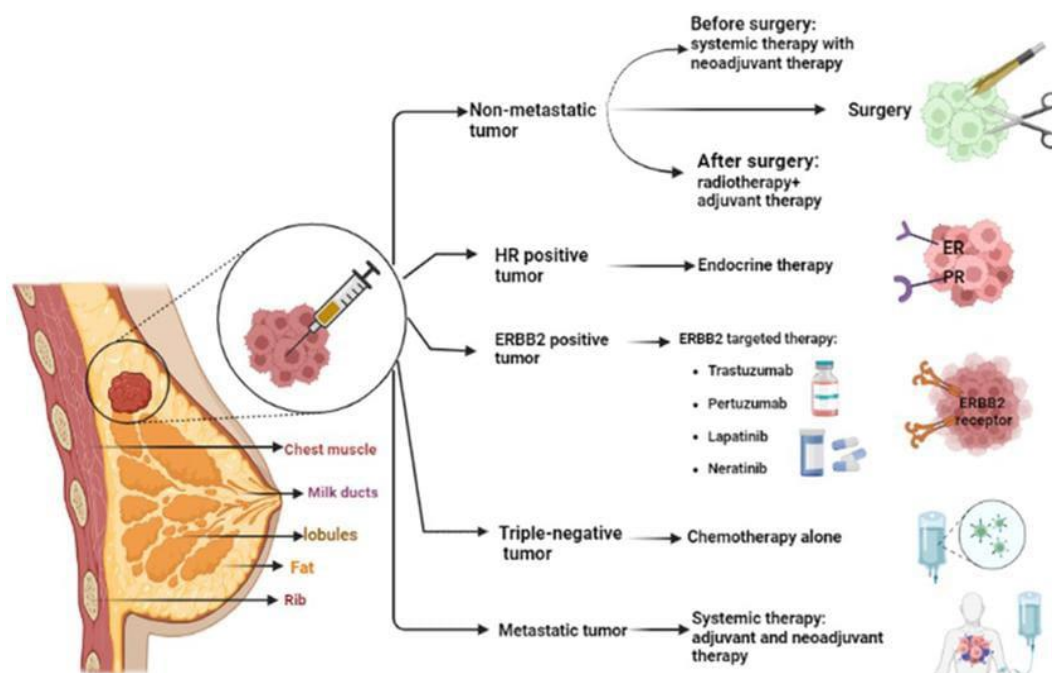


FIG. NO. 12: Treatment for Breast Cancer.

PHARMACOLOGICAL APPROACHES

1. Chemotherapy

Chemotherapy is widely used for treating breast cancer, especially when the disease is advanced or has a high risk of recurrence. Drugs like cyclophosphamide, doxorubicin, and paclitaxel are frequently used either alone or in combination.

2. Hormonal Therapy

For breast cancers that are hormone receptor-positive, treatments like tamoxifen (a selective estrogen receptor modulator) and aromatase inhibitors (e.g., letrozole, anastrozole) are commonly used to block estrogen, which can fuel cancer cell growth.

3. Targeted Therapy

For HER2-positive breast cancer, targeted therapies such as trastuzumab focus on blocking the HER2 protein, which accelerates cancer cell proliferation.

4. Immunotherapy

Immunotherapies, like pembrolizumab, are becoming increasingly important, especially for patients with triple-negative breast cancer, as they inhibit the PD-1 pathway to boost the immune system's attack on cancer cells.

NON-PHARMACOLOGICAL APPROACHES

1. Surgery

Surgery is often the primary approach for treating localized breast cancer. Depending on tumor characteristics, patients may undergo a lumpectomy (breast-conserving surgery) or a mastectomy (complete removal of the breast).

2. Radiation Therapy

Following surgery, radiation therapy is commonly used to reduce the chances of cancer returning, particularly after breast-conserving surgery.

3. Psychosocial Support

Non-pharmacological interventions also include psychological counseling and emotional support to help patients cope with the emotional impact of breast cancer, such as anxiety and depression.

4. Physical Therapy

Rehabilitation services for managing conditions like lymphedema and improving post-surgical mobility are important for enhancing the quality of life for breast cancer survivors.^[91-98]

F. TREATMENT OF HEPATIC CANCER

Hepatic cancer, commonly known as liver cancer, begins in the liver and is a leading cause of cancer-related deaths worldwide. It is particularly prevalent in areas with high rates of chronic liver diseases, such as hepatitis B and C infections.

The liver, a vital organ responsible for detoxification, metabolism, and nutrient storage, can develop primary cancers like hepatocellular carcinoma (HCC), the most common form. Other types include cholangiocarcinoma (bile duct cancer) and angiosarcoma. Additionally, liver cancer can occur as a secondary cancer, originating in another part of the body and spreading to the liver.

PHARMACOLOGICAL APPROACHES

1. Systemic Therapies

- **Sorafenib**: An oral multikinase inhibitor that was the first systemic agent approved for advanced HCC.

It has shown modest improvements in overall survival.

- **Lenvatinib:** Another first-line treatment option that has demonstrated non-inferiority to sorafenib in clinical trials.
- **Regorafenib:** Approved as a second-line treatment for patients who progress on sorafenib.

2. Immunotherapies

Agents such as nivolumab and pembrolizumab have been explored for HCC treatment.

3. Targeted Therapies

- **Atezolizumab plus Bevacizumab:** This combination has been found to improve both overall and progression-free survival compared to sorafenib alone.

NON-PHARMACOLOGICAL APPROACHES

1. Surgical Interventions

- **Partial Hepatectomy:** Surgical removal of the tumor is recommended for patients with sufficient hepatic function reserve. Five-year survival rates post-resection range from 41% to 74%.
- **Liver Transplantation:** Considered for patients with multiple hepatic lesions or severe underlying liver dysfunction, adhering to specific criteria such as the Milan criteria.

2. Ablation Techniques

- **Radiofrequency Ablation (RFA):** Utilizes high-frequency electrical currents to destroy cancer cells and is effective for small, localized tumors.
- **Microwave Ablation:** Similar to RFA but uses microwaves to generate heat, offering advantages in certain clinical scenarios.

3. Transarterial Therapies

- **Transarterial Chemoembolization (TACE):** Involves delivering chemotherapy directly to the liver tumor and blocking its blood supply.
- **Transarterial Radioembolization (TARE):** Delivers radioactive particles to the tumor via the hepatic artery, providing targeted radiation therapy.

4. Radiation Therapy

- **External Beam Radiation:** Used in select cases where other treatments are not feasible.^[99-103]

XIII. DIET AND NUTRITIONAL STATUS

Diet and nutritional status significantly impact cancer prevention, treatment, and recovery. Various cancers are influenced by different dietary factors, and maintaining proper nutrition can improve treatment outcomes. Below are key dietary influences and nutritional considerations for specific cancer types.

- **Colorectal Cancer**

Dietary Influences: A diet high in red and processed meats, low in fiber, and excessive alcohol consumption is

associated with an increased risk. In contrast, consuming ample fruits, vegetables, whole grains, and dairy products may offer protective benefits.

Nutritional Considerations: Many patients experience malnutrition due to treatment side effects like diarrhea and reduced appetite. A nutrient-dense diet with sufficient protein and calories is recommended to support recovery.

- **Breast Cancer**

Dietary Influences: Obesity and diets high in saturated fats have been linked to a greater risk of breast cancer. On the other hand, a Mediterranean-style diet, which includes olive oil, nuts, and fish, may provide protective effects.

Nutritional Considerations: Maintaining a healthy weight is essential, as excess body fat is associated with poorer outcomes. A diet rich in protein and antioxidants can help manage treatment-related side effects and promote recovery.

- **Lung Cancer**

Dietary Influences: A low intake of fruits and vegetables is correlated with an increased risk of lung cancer. However, high doses of beta-carotene supplements may be harmful, especially for smokers.

Nutritional Considerations: Patients often experience weight loss and muscle wasting (cachexia). A high-energy, high-protein diet, along with frequent small meals, can help manage these effects.

- **Prostate Cancer**

Dietary Influences: Diets high in dairy and excessive calcium intake have been linked to an increased risk of prostate cancer. Conversely, consuming lycopene-rich foods such as tomatoes and cruciferous vegetables may provide protective benefits.

Nutritional Considerations: A well-balanced diet that includes plant-based foods and lean proteins is recommended to support overall health and treatment efficacy.

- **Gastric (Stomach) Cancer**

Dietary Influences: High salt intake, frequent consumption of smoked foods, and infection with *Helicobacter pylori* are known risk factors. A diet rich in fresh fruits, vegetables, and vitamin C may help reduce the risk.

Nutritional Considerations: Many patients struggle with early satiety and weight loss. Consuming small, nutrient-dense meals and incorporating oral nutritional supplements can be beneficial.

• Pancreatic Cancer

Dietary Influences: The risk of pancreatic cancer is associated with high intake of processed meats and obesity, whereas diets rich in fruits, vegetables, and whole grains may have protective effects.

Nutritional Considerations: Malabsorption and significant weight loss are common in affected individuals. Strategies such as pancreatic enzyme replacement therapy and high-calorie diets can help manage symptoms and maintain nutrition.

• Liver Cancer

Dietary Influences: Consumption of aflatoxin-contaminated foods, excessive alcohol intake, and

obesity contribute to liver cancer risk. Diets rich in antioxidants and lean protein can support liver health.

Nutritional Considerations: Protein-energy malnutrition is frequently observed in liver cancer patients. A diet high in protein and avoidance of alcohol are crucial for maintaining nutritional status and overall health.^[104-110]

CONCLUSION

Cancer is a complex and multifaceted disease that affects millions of people worldwide. The various types of cancer, including hepatocellular carcinoma, ovarian cancer, head and neck cancer, and others, each have unique characteristics, risk factors, and treatment options.

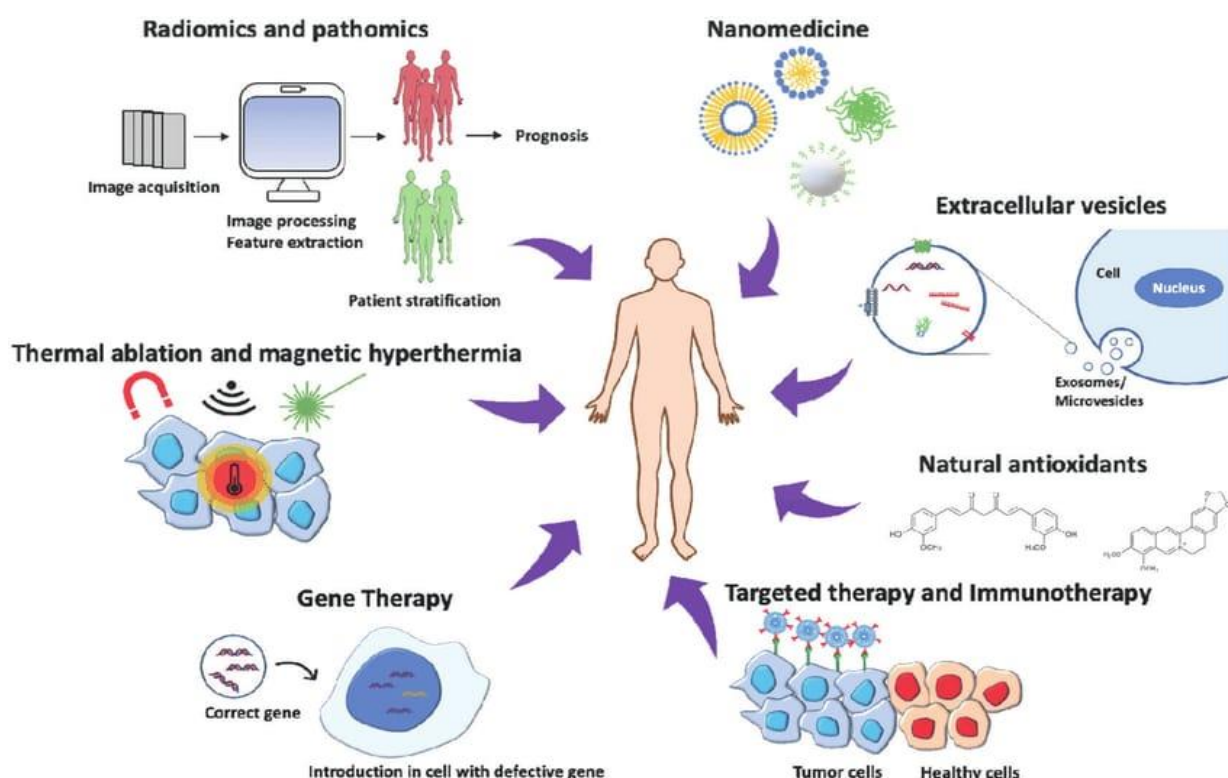


FIG.NO.13: Different therapies for Cancer.

Despite the differences between various types of cancer, there are several common themes that emerge.

1. Early detection is key: Early detection and diagnosis are critical for improving treatment outcomes and survival rates.

2. Multidisciplinary treatment approaches: Effective treatment often involves a combination of surgery, chemotherapy, radiation therapy, and other treatments.

3. Targeted therapies: Targeted therapies, such as immunotherapy and hormone therapy, offer promising new approaches for treating various types of cancer.

4. Importance of patient-centered care: Patient-centered care, including palliative care and supportive care, is essential for improving quality of life and treatment outcomes.

FUTURE DIRECTIONS

As research continues to advance our understanding of cancer biology and treatment options, several future directions emerge:

1. Precision medicine: Precision medicine approaches, including genomics and personalized medicine, hold promise for improving treatment outcomes.

2. Immunotherapy: Immunotherapy, including checkpoint inhibitors and cancer vaccines, is a rapidly evolving field with significant potential for improving treatment outcomes.

3. Combination therapies: Combination therapies, including combinations of targeted therapies and immunotherapies, offer promising new approaches for treating various types of cancer.

FINAL THOUGHTS

Cancer is a complex and multifaceted disease that requires a comprehensive and multidisciplinary approach to treatment. By continuing to advance our understanding of cancer biology and treatment options, we can improve treatment outcomes and quality of life for patients with cancer.^[111-113]

REFERENCE

1. National Cancer Institute. What is cancer? Bethesda: National Cancer Institute, 2022.
2. Jones M, Williams P. Understanding Carcinoma Subtypes. 3rd ed. New York : Medical press, 2020.
3. Hanahan D, Weinberg RA. Hallmarks of cancer: the next generation. *Cell*, 2011; 144(5): 646-74.
4. Chaffer CL, Weinberg RA. A perspective on cancer cell metastasis. *Science*, 2011; 331(6024): 1559-64.
5. Fares J, Fares MY, Khachfe HH, Salhab HA, Fares Y. Molecular principles of metastasis: a hallmark of cancer revisited. *Signal Transduct Target Ther*, 2020; 5(1): 28.
6. Lambert AW, Pattabiraman DR, Weinberg RA. Emerging biological principles of metastasis. *Cell*, 2017; 168(4): 670-91.
7. American Cancer Society. Cancer staging {Internet}. Atlanta (GA): American Cancer Society; 2022 [cited 2025 Feb 9].
8. 1.Hanahan D, Weinberg RA. Hallmarks of cancer: the next generation. *Cell*, 2011; 144(5): 646-74.
9. Vogelstein B, Kinzler KW. Cancer genes and the pathways they control. *Nat Med*, 2004; 10(8): 789-99.
10. Fidler IJ. The pathogenesis of cancer metastasis: the 'seed and soil' hypothesis revisited. *Nat Rev Cancer*, 2003; 3(6): 453-8.
11. Ferlay J, Colombet M, Soerjomataram I, Mathers C, Parkin DM, Piñeros M, et al. Estimating the global cancer incidence and mortality in 2018: GLOBOCAN sources and methods. *Int J Cancer*, 2019; 144(8): 1941-53.
12. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2020. *CA Cancer J Clin*, 2020; 70(1): 7-30.
13. Rubin AI, Chen EH, Ratner D. Basal-cell carcinoma. *N Engl J Med*, 2005; 353(21): 2262-9.
14. Knowles MA, Hurst CD. Molecular biology of bladder cancer: new insights into pathogenesis and clinical diversity. *Nat Rev Cancer*, 2015; 15(1): 25-41.
15. DeMarini DM. Genotoxicity of tobacco smoke and tobacco smoke condensate: a review. *Mutat Res*, 2004; 567(2-3): 447-74.
16. Nandakumar A, Ramnath T, Sureshkumar P, et al. Cancer statistics in India. *Indian J Cancer*, 2022; 59(3): 267-276.
17. Behera D, Balamugesh T. Lung cancer in India: a review. *Indian J Chest Dis Allied Sci*, 2022; 64(2): 77-86.
18. Sankaranarayanan R, Bhatla N, Gravitt PE, et al. Human papillomavirus infection and cervical cancer prevention in India. *Vaccine*, 2018; 36(32 Pt A): 4781-4791.
19. Mishra A, Mehta S, Sharma A, et al. Oral cancer in India: a review. *Indian J Dent Res*, 2022; 33(2): 151-158.
20. Zomawia E, Pala S, Sahoo S, et al. Cancer incidence in the North-East region of India. *Indian J Cancer*, 2022; 59(1): 35-42.
21. Kumar R, Singh AK, Singh PK, et al. Urban-rural differences in cancer incidence in India. *Indian J Cancer*, 2022; 59(3): 305-312.
22. American Cancer Society. Global Cancer Statistics, 2024. Atlanta: American Cancer Society, 2024.
23. National Centre for Disease Informatics And Research. World Cancer Day 2024: Close the Care Gap – Addressing Cancer Care in India. Bengaluru: NCDIR, 2024.
24. Cancerfax. Cancer Statistics in India, 2024.
25. Mid-Day. World Cancer Day 2025: Cancer Incidence Steadily Rising in India, Say Doctors. Mid-Day, 2024.
26. Worldwide Organization for Inquire about on Cancer. Tobacco Smoke and Automatic Smoking. IARC Monographs on the Assessment of Carcinogenic Dangers to People, 2004.
27. Worldwide Organization for Inquire about on Cancer. Radiation. IARC Monographs on the Assessment of Carcinogenic Dangers to People, 2012.
28. National Investigate Chamber. Wellbeing Dangers from Introduction to Moo Levels of Ionizing Radiation: BEIR VII Stage 2. National Foundations Press, 2006.
29. Lynch HT, Lynch PM, Lanspa SJ, et al. Audit of the Lynch Disorder: History, Atomic Hereditary qualities, Screening, Differential Conclusion, and Medicolegal Repercussions. *Clin Genet*, 2009; 76(1): 1-18.
30. Universal Office for Investigate on Cancer. Human Papillomaviruses. IARC Monographs on the Assessment of Carcinogenic Dangers to People, 2007.
31. Universal Office for Inquire about on Cancer. Schistosomes, Liver Flukes and Helicobacter pylori. IARC Monographs on the Assessment of Carcinogenic Dangers to People, 1994.
32. World Cancer Inquire about Finance, American Founded for Cancer Inquire about. Nourishment, Nourishment, Physical Action, and the Avoidance of Cancer: A Worldwide Viewpoint. AICR, 2007.
33. Worldwide Organization for Inquire about on Cancer. Weight Control and Physical Movement. IARC Monographs on the Assessment of Carcinogenic Dangers to People, 2002.
34. World Wellbeing Organization. Worldwide Suggestions on Physical Action for Wellbeing. WHO; 2010.
35. National Cancer Institute. Pain. Bethesda: National Cancer Institute, 2022.

36. American Cancer Society. Breast cancer symptoms. Atlanta: American Cancer Society, 2022.
37. Skin Cancer Foundation. Basal cell carcinoma. New York: Skin Cancer Foundation, 2022.
38. National Cancer Institute. Fever. Bethesda: National Cancer Institute, 2022.
39. National Cancer Institute. Neurological symptoms. Bethesda: National Cancer Institute, 2022.
40. American Cancer Society. Skin changes. Atlanta: American Cancer Society, 2022.
41. National Cancer Institute. Endocrine symptoms. Bethesda: National Cancer Institute, 2022.
42. Hanahan D, Weinberg RA. Hallmarks of cancer: the next generation. *Cell*, 2011; 144(5): 646-674.
43. Negrini S, Gorgoulis VG, Halazonetis TD. Genomic instability--an evolving hallmark of cancer. *Nat Rev Mol Cell Biol*, 2010; 11(3): 220-228.
44. Vogelstein B, Kinzler KW. Cancer genes and the pathways they control. *Nat Med*, 2004; 10(8): 789-799.
45. Johnstone RW, Ruefli AA, Lowe SW. Apoptosis: a link between cancer genetics and chemotherapy. *Cell*, 2002; 108(2): 153-164.
46. Folkman J. Angiogenesis. *Annu Rev Med*, 2006; 57: 1-18.
47. Zou W. Immunosuppressive networks in the tumour environment and their therapeutic relevance. *Nat Rev Cancer*. 2005; 5(4): 263-274.
48. Henderson BE, Feigelson HS. Hormonal carcinogenesis. *Carcinogenesis*, 2000; 21(3): 427-433.
49. Balkwill F, Mantovani A. Inflammation and cancer: back to Virchow? *Lancet*, 2001; 357(9255): 539-545.
50. International Agency for Research on Cancer. Tobacco smoke and involuntary smoking. *IARC Monogr Eval Carcinog Risks Hum*, 2004; 83: 1-1438.
51. World Health Organization. Global recommendations on physical activity for health. WHO, 2010.
52. World Cancer Research Fund, American Institute for Cancer Research. Food, nutrition, physical activity, and the prevention of cancer: a global perspective. AICR, 2007
53. Antoniou A, Pharoah PD, Narod S, et al. Average risks of breast and ovarian cancer associated with BRCA1 or BRCA2 mutations detected in case series unselected for family history: a combined analysis of 22 studies. *Am J Hum Genet*, 2003; 72(5): 1117-1130.
54. National Research Council. Health risks from exposure to low levels of ionizing radiation: BEIR VII Phase 2. National Academies Press, 2006.
55. International Agency for Research on Cancer. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. IARC, 2019
56. Leong SP, Shen ZZ, Liu TJ, Agarwal G, Tajima T, Paik NS, et al. Is breast cancer the same disease in Asian and Western countries? *World J Surg*, 2010; 34(10): 2308-24.
57. Ettinger DS, Wood DE, Aisner DL, Akerley W, Bauman JR, Chirieac LR, et al. Non-Small Cell Lung Cancer, Version 5.2017, NCCN Clinical Practice Guidelines in Oncology. *J Natl Compr Canc Netw*, 2017; 15(4): 504-35.
58. Siegel RL, Miller KD, Goding Sauer A, Fedewa SA, Butterly LF, Anderson JC, et al. Colorectal cancer statistics, 2020. *CA Cancer J Clin*, 2020; 70(3): 145-64.
59. Mottet N, van den Bergh RC, Briers E, Van den Broeck T, Cumberbatch MG, De Santis M, et al. EAU-EANM-ESTRO-ESUR-SIOG Guidelines on Prostate Cancer. *Eur Urol*, 2021; 79(2): 243-62.
60. Pui CH, Robison LL, Look AT. Acute lymphoblastic leukaemia. *Lancet*, 2008; 371(9617): 1030-43.
61. Henry NL, Hayes DF. Cancer biomarkers. *Mol Oncol*, 2012; 6(2): 140-146.
62. National Cancer Institute. (2022). Chemotherapy and You.
63. American Cancer Society. (2022). Radiation Therapy.
64. National Cancer Institute. (2022). Hormone Therapy.
65. American Cancer Society. (2022). Immunotherapy.
66. National Cancer Institute. (2022). Surgery.
67. Mottet N, Cornford P, van den Bergh RCN, Briers E, De Santis M, Fanti S, et al. EAU-EANM-ESTRO-ESUR-SIOG guidelines on prostate cancer. Part I: Screening, diagnosis, and local treatment with curative intent. *European Urology*, 2023; 84(3): 249-258.
68. Tannock IF, de Wit R, Berry WR, Horti J, Pluzanska A, Chi KN, et al. Docetaxel plus prednisone or mitoxantrone plus prednisone for advanced prostate cancer. *N Engl J Med*, 2004; 351(15): 1502-12.
69. de Bono JS, Oudard S, Ozguroglu M, Hansen S, Machiels JP, Kocak I, et al. Prednisone plus cabazitaxel or mitoxantrone for metastatic castration-resistant prostate cancer: a phase 3 trial. *Lancet*, 2010; 376(9747): 1147-54.
70. Kantoff PW, Halabi S, Conaway M, Picus J, Ragsdale SR, Hayes DF, et al. Hydrocortisone with or without mitoxantrone in men with hormone-refractory prostate cancer: results of the Cancer and Leukemia Group B 9182 study. *J Clin Oncol*, 1999; 17(8): 2506-13.
71. Sternberg CN, Petrylak DP, Madan RA. Progress in the treatment of advanced prostate cancer. *Am Soc Clin Oncol Educ Book*, 2014; (34): 117-31.
72. National Cancer Institute. (2020). Chemotherapy for lung cancer.
73. Herbst RS, Morgensztern D, Boshoff C. The biology and management of non-small cell lung cancer. *Nature*, 2018; 553(7689): 446-454.
74. Mok TS, Wu YL, Thongprasert S, et al. Gefitinib or carboplatin-paclitaxel in pulmonary adenocarcinoma. *N Engl J Med*, 2009; 361(10): 947-95.

75. Detterbeck FC, Chansky K, Groome P, et al. The IASLC Lung Cancer Staging Project: Proposals for revision of the M descriptors in the forthcoming eighth edition of the TNM classification for lung cancer. *J Thorac Oncol*, 2016; 11(1): 39–51.
76. Hanna N, Johnson D, Temin S, et al. Systemic therapy for stage IV non-small-cell lung cancer: American Society of Clinical Oncology clinical practice guideline update. *J Clin Oncol*, 2017; 35(30): 3484–3515.
77. Temel JS, Greer JA, Muzikansky A, et al. Early palliative care for patients with metastatic non-small-cell lung cancer. *N Engl J Med*. 2010; 363(8): 755–762.
78. Bray, F., et al. (2018). "Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries." *CA: A Cancer Journal for Clinicians*, 68(6), 394-424.
79. Dispenzieri, A., et al. (2018). "Immunotherapy for ovarian cancer: Emerging therapies and their potential clinical applications." *Gynecologic Oncology*, 149(1): 23-32.
80. Dunn, J., et al. (2017). "The psychosocial impact of ovarian cancer and the role of psychological interventions." *Journal of Clinical Oncology*, 35(30): 351-356.
81. Hennessy, B. T., et al. (2009). "Hormonal therapies in the treatment of ovarian cancer." *Nature Reviews Clinical Oncology*, 6(3): 145-155.
82. Jiang, W., et al. (2016). "Bevacizumab in the treatment of ovarian cancer: A systematic review." *Ovarian Cancer*, 4(1), 22-27.
83. Mulligan, J. K., et al. (2021). "Radiation therapy for ovarian cancer: Current and emerging strategies." *Current Treatment Options in Oncology*, 22(8): 71.
84. Pignata, S., et al. (2020). "Chemotherapy for advanced ovarian cancer: Current and future directions." *Cancer Treatment Reviews*, 83: 101945.
85. Wells, M., et al. (2017). "Nutrition and quality of life in ovarian cancer patients." *Cancer Nursing*, 40(4): E14-E24.
86. Ferris, R. L., Blumenschein, G. R., Fayette, J., Guigay, J., Colevas, A. D., Licitra, L., ... & Even, C. (2016). Nivolumab for recurrent squamous-cell carcinoma of the head and neck. *New England Journal of Medicine*, 375(19): 1856-1867.
87. Hanna, G. J., Salama, J. K., & Llorente, J. (2016). Management of head and neck cancer: Current concepts in radiotherapy. *Oncology*, 34(9): 53-60.
88. Salama, J. K., Vokes, E. E., & Burtness, B. (2019). Chemoradiotherapy for head and neck cancer. *American Journal of Clinical Oncology*, 42(5): 367-376.
89. Silverman, S. (2001). Oral cancer. *The Lancet*, 353(9147): 149-156.
90. Vogel, A., Garcia, J. F., & Kowalski, L. P. (2017). Advances in the radiotherapy treatment of head and neck cancers. *Seminars in Radiation Oncology*, 27(2): 155-164.
91. Barroso-Sousa, R., et al. (2020). "Immunotherapy in triple-negative breast cancer: Current status and future directions." *The Oncologist*, 25(1): e10-e21.
92. Early Breast Cancer Trialists' Collaborative Group. (2015). "Tamoxifen for early breast cancer: An overview of the randomized trials." *The Lancet*, 385(9976): 999-1005.
93. Fiorentino, L., et al. (2013). "Sleep disturbances and their impact on quality of life in breast cancer patients: A longitudinal study." *Journal of Clinical Oncology*, 31(17): 2215-2221.
94. Griguolo, G., et al. (2021). "Chemotherapy for breast cancer: Current and future perspectives." *Journal of Clinical Oncology*, 39(18): 1968-1979.
95. Hayes, S., et al. (2012). "Rehabilitation of upper limb lymphedema in breast cancer survivors: A comprehensive review." *Cancer Treatment Reviews*, 38(4): 431-439.
96. Morrow, M., et al. (2016). "Breast cancer surgery: The evolution of care." *JAMA Surgery*, 151(2): 130-135.
97. Slamon, D. J., et al. (2001). "Use of chemotherapy plus a monoclonal antibody against HER2 for metastatic breast cancer that overexpresses HER2." *New England Journal of Medicine*, 344(11): 783-792.
98. Vargo, J. A., et al. (2018). "Radiation therapy for breast cancer: Current perspectives." *Seminars in Radiation Oncology*, 28(2): 87-95.
99. Llovet JM, Ricci S, Mazzaferro V, Hilgard P, Gane E, Blanc JF, et al. Sorafenib in advanced hepatocellular carcinoma. *N Engl J Med*, 2008; 359(4): 378-90.
100. Finn RS, Qin S, Ikeda M, Galle PR, Ducreux M, Kim TY, et al. Atezolizumab plus bevacizumab in unresectable hepatocellular carcinoma. *N Engl J Med*, 2020; 382(20): 1894-905.
101. Bruix J, Qin S, Merle P, Granito A, Huang YH, Bodoky G, et al. Regorafenib for patients with hepatocellular carcinoma who progressed on sorafenib (RESORCE): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet*, 2017; 389(10064): 56-66.
102. Forner A, Reig M, Bruix J. Hepatocellular carcinoma. *Lancet*, 2018; 391(10127): 1301-14.
103. Kim E, Erhardt A. Current status of locoregional therapies in the treatment of hepatocellular carcinoma. *J Hepatol*, 2022; 76(5): 1225-38.
104. World Cancer Research Fund/American Institute for Cancer Research. Diet, nutrition, physical activity and colorectal cancer. Continuous Update Project Expert Report, 2018.
105. Farvid MS, Chen WY, Rosner BA, et al. Fruit and vegetable consumption and breast cancer incidence: repeated measures over 30 years. *Int J Cancer*, 2019; 144(7): 1496-510.
106. Alpha-Tocopherol, Beta Carotene Cancer Prevention Study Group. The effect of vitamin E and beta carotene on the incidence of lung cancer and other

- cancers in male smokers. *N Engl J Med*, 1994; 330(15): 1029-35.
107. Richman EL, Carroll PR, Chan JM. Vegetable and fruit intake after diagnosis and risk of prostate cancer progression. *Int J Cancer*, 2012; 131(1): 201-10.
108. González CA, Sala N, Rokkas T. Gastric cancer: epidemiologic aspects. *Helicobacter*, 2013; 18(Suppl 1): 34-8.
109. Molina-Montes E, Sánchez MJ, Buckland G, et al. Mediterranean diet adherence and risk of pancreatic cancer: a pooled analysis of three large European cohort studies. *Br J Cancer*, 2017; 116(5): 811-20.
110. World Cancer Research Fund. Diet, nutrition, physical activity and liver cancer. Continuous Update Project Report, 2015.
111. National Cancer Institute. (2022). Cancer Fact Sheets.
112. American Cancer Society. (2022). Cancer Facts & Figures.
113. World Health Organization. (2022). Cancer.