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# Cancer Overview

## Introduction

- Tumor: a mass of tissue formed via disruption of the normal cell cycle resulting in abnormal cell growth.
  - Benign: noncancerous due to the inability to invade neighboring tissues or spread to distant sites.
  - Malignant: cancerous due to ability to invade other tissues.
- Cancer: group of 100+ different diseases due to mutations in genetic material resulting in abnormal and uncontrolled cell growth.
- Metastasis: when cancer cells spread from the location of origin to another anatomical location.

Two main cancer classes and groupings:

	<b>Hematologic</b>		<b>Solid</b>
Leukemia	originates in blood-forming tissues, including bone marrow and spleen	Carcinoma	originates in major organs, skin, or tissues covering glands
Lymphoma	originates in the lymphatic system	Sarcoma	originates in connective tissue like muscle or bone, or soft tissues like adipose
Myeloma	originates in plasma cells		

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## Metastasis

Route	Definition	Common
Canalicular	spread via the anatomical canalicular spaces	carcinomas
Hematogenous	spread via bloodstream	sarcomas, renal cell, follicular thyroid, and hepatocellular carcinoma
Lymphatic	tumor cells reach regional lymph nodes and spread via the lymphatic system	carcinomas
Transcoelomic	malignancy spreads to body cavities via surface penetration of the peritoneal, pleural, pericardial, or subarachnoid spaces	ovarian

- Common during late-stage cancer and major contributor to morbidity and mortality.

Cancer-specific metastasis locations:

Cancer Type	Main Sites of Metastasis
Bladder	bone, liver, lung
Breast	bone, brain, liver, lung
Colon	liver, lung, peritoneum
Kidney	adrenal gland, bone, brain, liver, lung
Lung	adrenal gland, bone, brain, liver, other lung
Melanoma	bone, brain, liver, lung, skin, muscle
Ovary	liver, lung, peritoneum
Pancreas	liver, lung, peritoneum
Prostate	adrenal gland, bone, liver, lung
Rectal	liver, lung, peritoneum
Stomach	liver, lung, peritoneum
Thyroid	bone, liver, lung
Uterus	bone, liver, lung, peritoneum, vagina

## Cancer Overview

### General Statistics

- ≈1.9 million new cancer cases diagnosed in 2022 and 609,360 cancer deaths in the United States.
- Most commonly diagnosed cancers in 2022:

Male	Female
Prostate 27%	Breast 31%
Lung 12%	Lung 13%
Colorectal 8%	Colorectal 8%

Lowest 5-Year Survival	Highest 5-Year Survival
Mesothelioma 6.5%	Testicular cancer 95.3%
Pancreatic cancer 7.3%	Melanoma of skin 91.3%
Brain cancer 12.2%	Thyroid cancer 87.4%

### Cancer in the Emergency Department Statistics

- Emergency Department (ED) usage rate for cancer patients is more than double that of the general US population with ≈51% of visits resulting in hospital admission.

Time Frame from Diagnosis	ED Usage Rate
First 30 days	16%
First 6 months	35%
First year	44%

### Cancer Treatment Modalities

<b>Chemotherapy</b>	drugs given orally, infused, or injected that are cytotoxic and/or inhibit cell division
<b>Radiotherapy</b>	utilization of high dose radiation to kill and shrink tumors
<b>Targeted cell therapy</b>	precisely identifies and attacks specific cellular proteins and genes involved in cancer cell growth and survival

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<b>Hormone therapy</b>	targets individual hormones to slow or stop breast and prostate cancers that utilize these hormones for growth
<b>Immunotherapy</b>	assists immune system in fighting cancer either by amplifying or suppressing the innate immune response
<b>Surgery</b>	physical removal or debulking of the tumor
<b>Stem cell transplant</b>	replaces damaged stem cells with healthy ones from an unrelated or related donor, or from patients themselves

- Treatment for each patient may include one or more modalities at any given time.

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Main Chemotherapy Groups

Type	Mechanism
Alkylating agents	○ cause DNA strand crosslinking, abnormal base pairing, or strand breakage resulting in cell division inhibition
Plant alkaloids	○ <i>antimicrotubule agents</i> : Plant derivatives that inhibit mitosis by affecting the spindle function of microtubules ○ <i>topoisomerase inhibitors</i> : Plant derivatives that blocks enzymes that break and reconnect DNA strands required for cell division and growth
Antimetabolites	○ alter the function of enzymes required for protein synthesis and metabolism by mimicking nutrients used for cell growth so that the cancer cell eventually starves
Antitumor antibiotics	○ cause strands comprising DNA to uncoil inhibiting cell reproduction and therefore preventing RNA synthesis

Chemotherapy Types

Type	Examples	Cancers Treated	Common Side Effects
Alkylating agents	<i>Nitrogen mustard</i> : cyclophosphamide <i>Nitrosoureas</i> : carmustine <i>Alkylsulfonates</i> : busulfan <i>Hydrazines and Triazines</i> : dacarbazine <i>Ethylenimines</i> : thiotepa <i>Platinum based compounds</i> : cisplatin	leukemia, lymphoma, breast, lung, ovary, melanoma, multiple myeloma, sarcoma	myelosuppression, nausea/vomiting
Antimicrotubule agents	<i>Taxanes</i> : paclitaxel <i>Vinca alkaloids</i> : vincristine	myeloma, lymphoma, leukemia, breast, lung	peripheral neuropathy, myelosuppression

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Type	Examples	Cancers Treated	Common Side Effects
Topoisomerase inhibitors	<i>Topoisomerase I:</i> irinotecan <i>Topoisomerase II:</i> etoposide	leukemia, lung, gastrointestinal, ovarian, pancreatic	myelosuppression, nausea/vomiting, diarrhea
Antimetabolites	5-FU, gemcitabine, cytarabine, methotrexate, fludarabine	leukemia, breast, ovary, intestinal tract	myelosuppression, nausea/vomiting/diarrhea
Antitumor antibiotics	<i>Anthracyclines:</i> doxorubicin <i>Chromomycins:</i> dactinomycin <i>Miscellaneous:</i> bleomycin	broad spectrum solid and liquid tumors	cardiotoxicity, myelosuppression

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## Hematopoietic Stem Cell Transplantation

### Introduction

- Hematopoietic stem cells are immature blood cells made in the bone marrow that can mature into any blood cell type including white blood cells, platelets, and red blood cells.
- Hematopoietic stem cell transplantation (HSCT) for cancer treatment replaces dysfunctional bone marrow with healthy stem cells and destroys cancer cells in the process.
- HSCT can be classified by donor/recipient relationship into two types:

<b>Autologous</b>	<ul style="list-style-type: none"> <li>○ use of patient's own peripheral blood stem cells</li> <li>○ the goal is to eradicate residual cancer cells with intermediate resistance to standard chemotherapy</li> <li>○ cancer cells are killed by cytotoxicity</li> <li>○ no immune attack on cancer cells occurs</li> </ul>
<b>Allogenic</b>	<ul style="list-style-type: none"> <li>○ use of donor stem cells obtained from a related or unrelated blood donor or umbilical cord blood</li> <li>○ results in cancer cell destruction via two mechanisms:               <ul style="list-style-type: none"> <li>○ effects of cytotoxic chemotherapy</li> <li>○ graft-versus-tumor effect whereby donor's T cells attack residual cancer cells</li> </ul> </li> </ul>

HSCT is also classified by graft source:

Transplant Type	Graft Source
Peripheral blood stem cell transplant	Both autologous and allogenic
Cord blood transplant	Allogenic
Bone marrow transplant	Allogenic

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## Cancers Treated by HSCT

Autologous	Allogenic
Multiple myeloma	Acute myeloid leukemia
Light chain amyloidosis	Acute lymphoblastic leukemia
Non-Hodgkin's lymphoma	Chronic myeloid leukemia
Hodgkin's lymphoma	Myelodysplastic syndromes
Acute myeloid leukemia	Myeloproliferative disorders
Neuroblastoma	Non-Hodgkin's lymphoma
Germ cell tumors	Hodgkin's lymphoma
	Chronic lymphocytic leukemia
	Multiple myeloma

## Steps of the Stem Cell Transplant Process

<b>1. Harvesting</b>	Stem cells are harvested from the patient or the donor either from the peripheral blood stream or bone marrow
<b>2. Conditioning</b>	Chemotherapy and/or radiation is administered to the recipient to destroy cancer cells in the body and create room in the bone marrow for a population of transplanted stem cells
<b>3. Transplant</b>	Recipient receives stem cells via IV infusion
<b>4. Engraftment and Recovery</b>	Transplanted stem cells grow and produce healthy blood cells in the recipient Approximate time course: Peripheral and bone marrow stem cells 2–3 weeks Cord blood stem cells 3–5 weeks

## HSCT Complications

Divided into three categories based on timing:

Name	Time Course	Complications
<b>Pre-engraftment period</b>	From start of conditioning regimen to neutrophil recovery	<ul style="list-style-type: none"> <li>○ pancytopenias</li> <li>○ infection: related to neutropenia consisting of gram-positive and gram-negative bacteria, herpes simplex virus, candidiasis, and invasive aspergillosis</li> <li>○ organ dysfunction</li> </ul>

## Hematopoietic Stem Cell Transplantation

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Name	Time Course	Complications
<b>Early post-engraftment period</b>	From neutrophil recovery to day 100	<ul style="list-style-type: none"> <li>○ acute GvHD</li> <li>○ infection from impaired cellular and humoral immunity: opportunistic infections such as <i>Pneumocystis jirovecii</i> and cytomegalovirus</li> <li>○ treatment of GvHD causes immunosuppression increasing the risk of invasive fungal infections and viral reactivation</li> </ul>
<b>Late post-engraftment period</b>	From day 100 and beyond	<ul style="list-style-type: none"> <li>○ chronic GvHD: most commonly skin is affected but it also affects other sites such as connective tissue, muscle, eye, mouth, lungs, and GI tract</li> </ul>

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## Hormone Therapy

## Introduction

- Hormone therapy is a systemic treatment targeting certain types of breast and prostate cancers that are dependent on specific hormones for growth.
- Treatment can be used to slow or stop cancer cell growth and/or lessen specific cancer-related symptoms.
- The mechanism of delivery can be via oral ingestion, intramuscular or subcutaneous injections, or surgical removal or hormone synthesizing organs.

## Examples of Hormone Therapy

Type	Examples	Cancer Types
Progestins	megestrol acetate	endometrial
Selective estrogen receptor modulators	tamoxifen, raloxifene	endometrial, breast, adrenal
Luteinizing hormone-releasing agonists	goserelin, leuprolide,	endometrial, breast, prostate
Aromatase inhibitors	anastrozole, exemestane	endometrial, breast
Estrogen receptor antagonists	fulvestrant, toremifene	breast, adrenal
Surgical removal	oophorectomy, orchiectomy	breast, prostate
Antiandrogens	apalutamide, nilutamide	prostate
CYP17 inhibitors	abiraterone	prostate
Adrenolytic	mitotate	adrenal