

Approach to the Patient with Cancer

(See also *Harrison's Principles of Internal Medicine*, 17th Edition, Chapter 77)

Definition

- Cancer includes various types of malignant neoplasms caused by abnormal or uncontrolled cell growth.
- This topic covers the general approach to patients with cancer.
 - See individual cancers for details specific to each type.

Epidemiology

Overall incidence

- In 2007
 - 1,444,920 new cases of invasive cancer diagnosed
 - Men: 766,860 cases
 - Women: 678,060 cases
 - 559,650 deaths cancer
 - Men: 289,550
 - Women: 270,100
- Cancer incidence has been decreasing by about 2% each year since 1992.
- Race
 - Incidence varies among racial and ethnic groups.
 - The basis for these differences is unclear.

Incidence, by type

- Men
 - Prostate: 33%
 - Lung and bronchus: 13%
 - Colon and rectum: 10%
 - Bladder: 7%
 - Melanoma: 5%
 - Lymphoma: 4%
 - Kidney: 3%
 - Leukemia: 3%
 - Oral cavity: 3%
 - Pancreas: 2%
 - All other: 17%
- Women
 - Breast: 32%
 - Lung and bronchus: 12%
 - Colon and rectum: 11%

- Endometrium: 6%
- Lymphoma: 4%
- Melanoma: 4%
- Ovary: 3%
- Thyroid: 3%
- Pancreas: 2%
- Bladder: 2%
- All other: 21%

Deaths from cancer

- Men
 - Lung and bronchus: 31%
 - Prostate: 10%
 - Colon and rectum: 10%
 - Pancreas: 5%
 - Leukemia: 4%
 - Esophagus: 4%
 - Liver and bile duct: 3%
 - Lymphoma: 3%
 - Bladder: 3%
 - Kidney: 3%
 - All other: 24%
- Women
 - Lung and bronchus: 27%
 - Breast: 15%
 - Colon and rectum: 10%
 - Ovary: 6%
 - Pancreas: 6%
 - Leukemia: 4%
 - Lymphoma: 3%
 - Endometrium: 3%
 - Myeloma: 2%
 - Brain: 2%
 - All other: 21%
- Cancer surpassed heart disease as the leading cause of death in people ≤ 85 years of age beginning in 1999.
 - Among persons > 85 years, cancer is the second leading cause of death (behind heart disease).
 - The cancer death rate began to decrease in 1992.
 - Death rate in men has decreased 1.5% per year.
 - Death rate in women has decreased 0.8% per year.

Risk Factors

- The most significant risk factor for cancer overall is age.
 - Two-thirds of all cases are in persons > 65 years of age.
 - Cancer incidence increases as the third, fourth, or fifth power of age in different sites.
- Other important risk factors
 - Smoking
 - Family history

- Occupational exposure
- Sun exposure

Etiology

- Exact mechanisms are not fully understood and are largely dependent on the underlying cancer.
- 2 cardinal features of cancer
 - Abnormal or uncontrolled cell growth; carcinogenesis is the process that transforms a normal cell to a cancer cell.
 - Multistep process
 - Involves genetic alterations leading to alterations in DNA affecting cell
 - Growth
 - Repair
 - Energy production
 - Senescence
 - Cell suicide
 - Genetic change can occur in a variety of genes (≥ 10).
 - Activating mutations of an oncogene that drives tumor growth
 - Inactivating mutations of a tumor suppressor gene
 - Chromosome translocations that alter gene expression or create a new gene product
 - Alterations in epigenetic mechanisms controlling gene expression, such as loss of methylation of an imprinted gene
 - Tissue invasion and metastasis

Symptoms & Signs

- Signs and symptoms relate to the underlying cancer.
- General signs and symptoms include unexplained:
 - Weight loss
 - Fever
 - Fatigue
 - Night sweats
 - Pain
 - Changes in the skin
 - Mass or swelling
 - Loss of function

Differential Diagnosis

- Differential diagnosis varies depending on clinical presentation and underlying cancer.

Diagnostic Approach

- The diagnosis of cancer relies most heavily on invasive tissue biopsy and should never be made without obtaining tissue.
- Occasionally a patient will present with a metastatic disease process that is defined as cancer on biopsy but has no apparent primary site of disease.
 - Efforts should be made to define the primary site on the basis of:
 - Age
 - Sex

- Sites of involvement
 - Histology and tumor markers
 - Personal and family history
 - Particular attention should be focused on ruling out the most treatable cause.
- Assemble a multidisciplinary team.
 - Primary care physician
 - Medical oncologist
 - Surgical oncologist
 - Radiation oncologist
 - Oncology nurse specialist
 - Pharmacist
 - Social worker
 - Rehabilitation medicine specialist
 - Other consulting professionals
- Define extent of disease and prognosis.
 - Staging
 - Clinical staging: physical examination, radiographs, isotopic scans, CT and other imaging procedures
 - Pathologic staging: histologic examination of all tissues removed during a surgical procedure
 - The most widely used system of staging is the TNM (tumor, node, metastasis) system (see Classification).
 - Assess the physiologic reserve of the patient.
 - Age
 - Karnofsky performance status (<70 indicates poor prognosis)
 - 100: Normal, no complaints, no evidence of disease
 - 90: Able to carry on normal activity; minor signs and symptoms of disease
 - 80: Normal activity with effort; some signs and symptoms of disease
 - 70: Cares for self; unable to carry on normal activity or do active work
 - 60: Requires occasional assistance but is able to care for most of needs
 - 50: Requires considerable assistance and frequent medical care
 - 40: Disabled; requires special care and assistance
 - 30: Severely disabled; hospitalization is indicated although death is not imminent
 - 20: Very sick; hospitalization necessary; active supportive treatment is necessary
 - 10: Moribund, fatal processes progressing rapidly
 - 0: Dead
 - Biological features of tumor
 - Expression of particular oncogenes
 - Drug-resistance genes
 - Apoptosis-related genes
 - Genes involved in metastasis are being found to influence response to therapy and prognosis.

Laboratory Tests

- A battery of laboratory tests are used during diagnosis and follow-up.
 - Depend on underlying cancer

Imaging

- Depend on underlying cancer
- In addition to physical examination, clinical staging is based on:
 - Radiographs
 - Isotopic scans
 - CT or MRI
 - Other imaging procedures

Diagnostic Procedures

- Biopsy
 - The diagnosis of cancer relies most heavily on invasive tissue biopsy and should never be made without obtaining tissue.

Classification

- The most widely used system of staging is the TNM (tumor, node, metastasis) system.
- Codified by the International Union Against Cancer and the American Joint Committee on Cancer
- Categorizes tumors on the basis of:
 - Size of the primary tumor/lesion
 - T 1–4, where a higher number indicates a larger tumor
 - Presence of nodal involvement
 - Usually N0 and N1 for the absence and presence, respectively, of involved nodes
 - Some tumors have more elaborate systems of nodal grading.
 - Presence of metastatic disease
 - M0 and M1 for the absence and presence, respectively, of metastases
 - Various permutations of T, N and M are broken into stages, usually designated I–IV.
 - Tumor burden increases and curability decreases with increasing stages.
- Other anatomic staging systems for some tumors
 - Dukes classification for colorectal cancer
 - The International Federation of Gynecologists and Obstetricians classification for gynecologic cancers
 - Ann Arbor classification for Hodgkin's disease
- For certain tumors (e.g., those of hematopoietic origin), clinical features are more important than anatomic staging for assessing prognosis.

Treatment Approach

Initial steps

- Create a treatment plan.
 - Determine whether treatment approach should be curative or palliative.
 - Use standard treatment protocols or ongoing clinical research protocols.
 - Avoid ad hoc alterations of defined treatment regimens that are not a component of a research study.
 - Avoid anticipatory dose modifications or treatment delays that have not been dictated by a toxicity or complication actually encountered.

Management

- Manage disease and treatment complications.
- Assess response to treatment.
 - Categories of response
 - Complete response: disappearance of all evidence of disease
 - Partial response: >50% reduction in the sum of the products of the perpendicular diameters of all measurable lesions
 - Progressive disease: appearance of any new lesion or an increase >25% in the sum of the products of the perpendicular diameters of all measurable lesions
 - Stable disease: tumor shrinkage or growth that does not meet any of these criteria
 - Response Evaluation Criteria in Solid Tumors (RECIST) Criteria
 - Complete response: same as above
 - Partial response: 30% decrease in the sums of the longest diameters
 - Progressive disease: 20% or greater increase in the sums of the longest diameters
 - Stable disease: change that does not meet any of these criteria
- Maintain quality of life by treating:
 - Pain
 - 25–50% of patients present with pain at diagnosis.
 - 33% have pain associated with treatment.
 - 75% have pain with progressive disease.
 - Nausea
 - Acute emesis: most common, occurs with 24 hours of treatment
 - Delayed emesis: occurs within 1–7 days after treatment
 - Anticipatory emesis: occurs before the delivery of chemotherapy
 - Effusions
 - Asymptomatic malignant effusions may not require treatment.
 - Symptomatic effusions in tumors responsive to systemic therapy usually do not require local treatment but respond to the treatment for the underlying tumor.
 - Symptomatic effusions in tumors unresponsive to systemic therapy may require local treatment in patients with a life expectancy ≥ 6 months.
 - Nutrition
 - It remains controversial how to assess nutritional status and when and how to intervene.
 - Use a prognostic nutritional index based on:
 - Albumin levels
 - Triceps skin-fold thickness
 - Transferrin levels
 - Delayed-type hypersensitivity skin test
 - Or, use a defined threshold for nutritional intervention.
 - >10% unexplained body weight loss
 - Serum transferrin level <1,500 mg/L (150 mg/dL)
 - Serum albumin level <34g/L (3.4 g/dL)
 - Psychological support for:
 - Depression
 - Incidence is about 25% overall in patients with cancer.
 - Cosmetic changes
 - Loss of control over life
 - Sexual dysfunction

- Survivor guilt
- Damocles syndrome (fear of relapse)

End-of-life decisions

- Speak frankly with patient and family about course of disease.
- Determine whether patient would prefer home or hospice care.
- Ask patient for advanced directive and review periodically.

Specific Treatments

Disease management

- Treatment is specific to the type of cancer, as well as stage.
- Treatment options
 - Surgery
 - Radiation
 - Chemotherapy
 - Biological therapy
 - A combination of the above

Supportive care

Depression

- Serotonin reuptake inhibitor
 - Fluoxetine (10–20 mg/d)
 - Sertraline (50–150 mg/d)
 - Paroxetine (10–20 mg/d)
- Tricyclic antidepressant
 - Amitriptyline (50–100 mg/d)
 - Desipramine (75–150 mg/d)
- Allow 4–6 weeks for response.
- Effective therapy should be continued \geq 6 months after resolution of symptoms.
- If therapy is unsuccessful, other classes of antidepressants may be used.
- In addition to medication, psychosocial interventions may be of benefit.
 - Support groups
 - Psychotherapy
 - Guided imagery

Pain

- Pharmacologic intervention
- Antitumor therapy
- Neurostimulatory techniques
- Regional analgesia
- Neuroablative procedures

Nausea

- Tailor to the patient's situation.
- For mildly and moderately emetogenic agents
 - Prochlorperazine, 5–10 mg PO or 25 mg rectally
 - Efficacy may be enhanced by administering the drug before chemotherapy is delivered.
 - Dexamethasone, 10–20 mg IV, is also effective and may enhance the efficacy of prochlorperazine.
- For highly emetogenic agents (e.g., cisplatin, mechlorethamine, dacarbazine, streptozocin)
 - Combinations of agents work best, and administration should begin 6–24 hours before treatment.
 - Ondansetron, 8 mg PO every 6 hours the day before therapy and IV on the day of therapy, plus dexamethasone, 20 mg IV before treatment
 - Addition of oral aprepitant (a substance P/neurokinin 1 receptor antagonist) to this regimen (125 mg on day 1, 80 mg on days 2 and 3) further decreases the risk of acute and delayed vomiting.
- Delayed emesis
 - Oral dexamethasone and oral metoclopramide
- The best strategy for preventing anticipatory emesis is to control emesis in the early cycles of therapy, to prevent the conditioning from taking place.

Effusions

- Symptomatic pleural effusions
 - Thoracentesis is usually performed first; in most cases, symptomatic improvement occurs for < 1 month.
 - Chest tube drainage is required if symptoms recur within 2 weeks.
 - Sclerosis with bleomycin or doxycycline
- Symptomatic pericardial effusions
 - Pericardial window **or**
 - Stripping the pericardium
 - If the patient's condition does not permit surgery procedure, sclerosis can be attempted with doxycycline and/or bleomycin.
- Malignant ascites
 - Repeated paracentesis of small volumes of fluid
 - If the underlying malignancy is unresponsive to systemic therapy, peritoneovenous shunts may be inserted.

Nutrition

- Enteral nutrition provided orally or by tube feeding is preferred over parenteral supplementation.
- Megestrol acetate

Monitoring

- Assess response to treatment.
 - Careful physical examination
 - Periodic imaging studies

- If imaging studies have become normal, repeat biopsy of previously involved tissue to document complete response by pathologic criteria.
 - Biopsies are not usually required if there is macroscopic residual disease.
 - Exceptions include testicular cancer, where residual mass may be benign teratoma, and Hodgkin's disease, where residual mass may be scar.
- Tumor markers may be useful in certain tumors.
 - Human chorionic gonadotropin: gestational trophoblastic disease, gonadal germ-cell tumor
 - Calcitonin: medullary cancer of the thyroid
 - Catecholamines: pheochromocytoma
 - α -Fetoprotein: hepatocellular carcinoma, gonadal germ-cell tumor
 - Carcinoembryonic antigen: adenocarcinoma of the colon, pancreas, lung, breast, ovary
 - Prostatic acid phosphatase: prostate cancer
 - Neuron-specific enolase: small-cell cancer of the lung, neuroblastoma
 - Lactate dehydrogenase: lymphoma, Ewing's sarcoma
 - Prostate-specific antigen: prostate cancer
 - Monoclonal immunoglobulin: myeloma
 - CA-125: ovarian cancer, some lymphomas
 - CA 19-9: colon, pancreatic, breast cancer
 - CD30: Hodgkin's disease, anaplastic large-cell lymphoma
 - CD25: hairy-cell leukemia, adult T-cell leukemia/lymphoma
 - β_2 -Microglobulin: myeloma, lymphoma
- At completion of treatment
 - If patient is free of disease, follow regularly for disease recurrence.
 - If patient is not free of disease, consider salvage therapy.

Complications

- Most common complications of cancer therapy
 - Nausea and vomiting
 - Febrile neutropenia
 - Myelosuppression
- Other complications of cancer and its therapy
 - Depression
 - Pain
 - Nausea
 - Nutritional problems and weight loss
 - Effusions
 - Fatigue
 - Sleep disturbances

Prognosis

- Current treatment techniques result in cure of >50% of patients diagnosed with cancer.
- 5-year survival rate for white patients
 - 39% in 1960–1963
 - 64% in 1992–1998
- 5-year survival rate for African-American patients
 - 53% in 1992–1998
- Basis for variable mortality rate among racial and ethnic groups remains unclear.

- Most common causes of death in patients with cancer
 - Infection (leading to circulatory failure)
 - Respiratory failure
 - Hepatic failure
 - Renal failure

Prevention

- Preventive strategies focus on risk factor modification.
 - Smoking cessation
 - Diet modification
 - Sun avoidance
- Early detection
 - Routine health screening

ICD-9-CM

- 199.1 Other malignant neoplasm without specification of site
- 234.9 Carcinoma in situ of other and unspecified sites, site unspecified Approach to the Patient with Cancer

See Also

- Acute Lymphoid Leukemia
- Acute Myeloid Leukemia
- Adrenal Cancer
- Anal Cancer
- Anemia of Chronic Disease
- Approach to Weight Loss
- Basal-Cell Cancer of the Skin
- Benign Prostatic Hyperplasia
- Bladder cancer
- Breast Cancer
- Cancer of the Liver
- Cancer of the Stomach
- Cancer Screening and Prevention
- Carcinoid Tumors
- Central Nervous System Tumors
- Cervical Cancer
- Chronic Lymphoid Leukemia
- Chronic Myeloid Leukemia
- Colorectal Cancer
- Endometrial Cancer
- Esophageal Cancer
- Gastrointestinal Bleeding
- Gynecomastia
- Head and Neck Cancer
- Hemoptysis
- Hodgkin's Disease
- Hypercalcemia of Malignancy
- Intestinal Obstruction in the Cancer Patient
- Late Consequences of Cancer and Its Treatment

- Lung Cancer, General
- Lymphadenopathy
- Malignant Spinal Cord Compression
- Management of Cancer Pain
- Management of Malignant Effusions
- Meningioma
- Metastatic Cancer of Unknown Primary
- Multinodular Goiter
- Nausea and Vomiting
- Neutropenia
- Non-Hodgkin Lymphomas
- Non-Small Cell Lung Cancer
- Ovarian Cancer
- Pancreatic Cancer
- Paraneoplastic Hyponatremia
- Pheochromocytoma
- Prostate Cancer
- Renal Cancer
- Small-Cell Lung Cancer
- Soft-Tissue Sarcomas
- Solitary Pulmonary Nodule
- Solitary Thyroid Nodule
- Splenomegaly
- Squamous-Cell Cancer of the Skin
- Superior Vena Cava Syndrome
- Testicular Cancer
- Thyroid Cancer
- Tumor Lysis Syndrome
- Weight Loss

Internet Sites

- Professionals
 - Research and Funding
National Cancer Institute
 - Information for Professionals
American Cancer Society
- Patients
 - Homepage
American Cancer Society
 - Cancer topics
National Cancer Institute
 - Finding clinical trials
National Cancer Institute

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PEARLS

- Patients with cancer can also develop conditions that are unrelated to cancer.
 - It is important that the cause of symptoms be evaluated carefully and reversible causes ruled out rather than to assume that a new symptom reflects progressive cancer growth.
- Cancer may present as migratory thrombophlebitis (Trousseau's syndrome).
- Even when the goal of cancer care has become palliation, it is critical for the physician to continue to spend time with the patient.
 - Hospitalized patients should be examined each day.
 - Go into the room and speak with the patient.
 - Sit down and listen to what the patient wants to say.
 - Ask if he or she needs anything.
 - Avoiding a dying patient is the worst possible approach to his/her care.
- Opioids should not be withheld from a patient with cancer who is in pain because of a misplaced fear of addiction.
 - Addiction in the setting of cancer pain is very rare.
- When a fever is due to occult cancer, the most common causative cancers are hepatocellular carcinoma, renal-cell carcinoma, and lymphoma.
- The most treatable cancers that present as cancer of unknown primary site are extragonadal germ-cell tumors, lymphomas, breast cancers, and prostate cancers.