

## 125 Late Consequences of Cancer and Its Treatment

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There are over 10 million American cancer survivors. The vast majority of these will bear some mark of their cancer and its treatment, and a large proportion will experience long-term consequences including medical problems, psychosocial dysfunction, economic hardship, sexual dysfunction, and discrimination regarding employment and insurance. Many of these problems are directly related to cancer treatment. As patients survive longer from more types of malignancies, we are increasingly recognizing the biologic toll our very imperfect therapies take in terms of morbidity and mortality. The human face of these consequences of therapy confronts the cancer specialist who treats them every day. Although long-term survivors of childhood leukemias, Hodgkin's lymphoma, and testicular cancer, as examples, have taught us much about the consequences of cancer treatment, we keep learning more as patients survive longer with newer therapies. Newer "targeted" chemotherapy drugs have their own, often unique, long-term toxicities about which we remain in a learning process. Cancer "survivorship" clinics are increasing to expressly follow patients for long-term toxicities of cancer treatment.

The pace of developing therapies that mitigate treatment-related consequences has been slow, partly due to an understandable aversion to alter regimens that work and partly due to a lack of new, effective, less toxic therapeutic agents with less "collateral damage" to replace known agents with known toxicities. The types of damage from

cancer treatment vary. Often, a final common pathway is irreparable damage to DNA. Surgery can create dysfunction, including blind gut loops with absorption problems and loss of function of removed body parts. Radiation may damage end-organ function, for example, loss of potency in prostate cancer patients, pulmonary fibrosis, and neurocognitive impairment, and may act as a direct carcinogen. Cancer chemotherapy can be a direct carcinogen and has a kaleidoscope of other toxicities discussed in this chapter. **Table 125-1** lists the late effects of cancer treatment.

**TABLE 125-1 LATE EFFECTS OF CANCER THERAPY**

| Surgical Procedure    |                                  | Effect                                             |
|-----------------------|----------------------------------|----------------------------------------------------|
| Amputation            |                                  | Functional loss                                    |
| Lymph node dissection |                                  | Risk of lymphedema                                 |
| Ostomy                |                                  | Psychosocial impact                                |
| Splenectomy           |                                  | Risk of sepsis                                     |
| Adhesions             |                                  | Risk of obstruction                                |
| Bowel anastomoses     |                                  | Malabsorption syndromes                            |
| Radiation Therapy     |                                  | Effect                                             |
| Organ                 |                                  |                                                    |
| Bone                  |                                  | Premature termination of growth, osteonecrosis     |
| Soft tissues          |                                  | Atrophy, fibrosis                                  |
| Brain                 |                                  | Neuropsychiatric deficits, cognitive dysfunction   |
| Thyroid               |                                  | Hypothyroidism, Graves' disease, cancer            |
| Salivary glands       |                                  | Dry mouth, caries, dysgeusia                       |
| Eyes                  |                                  | Cataracts                                          |
| Heart                 |                                  | Pericarditis, myocarditis, coronary artery disease |
| Lung                  |                                  | Pulmonary fibrosis                                 |
| Kidney                |                                  | Decreased function, hypertension                   |
| Liver                 |                                  | Decreased function                                 |
| Intestine             |                                  | Malabsorption, stricture                           |
| Gonads                |                                  | Infertility, premature menopause                   |
| Any                   |                                  | Secondary neoplasia                                |
| Chemotherapy          |                                  | Effect                                             |
| Organ                 | Drug                             |                                                    |
| Bone                  | Glucocorticoids                  | Osteoporosis, avascular necrosis                   |
| Brain                 | Methotrexate, cytarabine, others | Neuropsychiatric deficits, cognitive decline?      |
| Peripheral nerves     | Vincristine, platinum, taxanes   | Neuropathy, hearing loss                           |
| Eyes                  | Glucocorticoids                  | Cataracts                                          |
| Heart                 | Anthracyclines, trastuzumab      | Cardiomyopathy                                     |
| Lung                  | Bleomycin                        | Pulmonary fibrosis                                 |
|                       | Methotrexate                     | Pulmonary hypersensitivity                         |
| Kidney                | Platinum, others                 | Decreased function, hypomagnesemia                 |
| Liver                 | Various                          | Altered function                                   |
| Gonads                | Alkylating agents, others        | Infertility, premature menopause                   |
| Bone marrow           | Various                          | Aplasia, myelodysplasia, secondary leukemia        |