Cancer pain patients commonly experience more than one kind of pain. The pain may be constant or intermittent, or acute pain superimposed on chronic background pain. The pain may be disease-related or treatment-related. Chronic pain conditions, such as low back pain, that were present prior to the cancer may also continue to be problematic. Psychological factors such as depression, anxiety, and cognitive style may influence pain perception and contribute to the intensity of the pain.

Multiple Causes of Pain in the Cancer Patient
- Tumor expansion can cause pressure on surrounding organs.
- Tumors secrete inflammatory and prohyperalgesic mediators.
- Tumor infiltration in nerve plexuses and damage to nerve tissue can cause neuropathic pain.
- Metastatic spread of cancer to bone is one of the most common causes of cancer pain [1].
- Stretching of hollow viscera, distortion of the capsule of solid organs, inflammation of the mucosa, and ischemia or necrosis activate visceral nociceptors, resulting in visceral pain.
- Rapid weight loss, muscle hypercatabolism, immobilization, or increased muscular tension cause muscular pain. Bony metastases can cause painful muscle spasm.
- Breakthrough pain, defined as a transitory flare of pain that occurs on a background of relatively well-controlled baseline pain [2], is prevalent. It may be due to a number of causes, such as bony metastases causing pain on movement.

Treatment-Related Pain
- Adverse effects of treatment include joint pain following chemotherapy and hormonal therapy, and painful mucositis due to radiotherapy and chemotherapy with certain agents. Neuropathic pain may arise in the form of postradiation plexopathies, peripheral polyneuropathy after chemotherapy, or opioid-induced hyperalgesia.
- Surgical interventions can give rise to nerve damage and chronic postoperative pain.

Pathophysiology
The pathophysiology of cancer pain is complex and includes:
- Local and systemic inflammatory response, with production of pro-inflammatory cytokines, which facilitate pain transmission.
- Directly tumor-related pain [3]: Cancer cells can cause invasion of mechanically sensitive tissues (e.g., visceral pain) or entrapment and injury of nerves (e.g., neuropathic pain). Tumors contain immune-system cells that release factors including endothelin, prostaglandins, and tumor necrosis factor alpha (TNF-α), which excite or sensitize peripheral nociceptive primary afferents. Tumors release protons, causing local acidosis, with similar effects. The ongoing pain induces and may be partially maintained by a state of central sensitization. Proteolytic enzymes produced by tumor cells can damage sensory and sympathetic nerve fibers, causing neuropathic pain.
- Metastatic cancer-induced bone pain [4,5]: Injury or infiltration of sensory neurons that innervate the bone marrow cause pain. Alterations in normal bone turnover occur, with loss of mechanisms that normally regulate the balance between osteoclast and osteoblast activity. With advanced disease, the bone loses mechanical strength and is subject to osteolysis, pathological fracture, and microfractures. Mechanical distortion of the peristeum may be a major source of pain.
- Neuropathy: Chemotherapy-associated neuropathy arises due to different mechanisms, including disruption of tubulin function by chemotherapeutic agents, with release of cytokines, resulting in degeneration of sensory neurons and sensitization of primary nociceptive afferents [3]. Radiotherapy can cause tissue fibrosis with nerve compression and microvascular obstruction of the nerve. Nervous tissue compression or lesion contributes to central sensitization.
References