16.1 Introduction

Some of the most common late effects of therapy involve the musculoskeletal skeletal system. While the growth deficits of radiation are well known, it is important to realize that surgery and sometimes chemotherapy affect the developing musculoskeletal system as well. In general, the treatment of sarcomas leads to the most severe late effects with all therapies because the underlying malignancy originates in a muscle or bone, and often an extremity. In spite of the advances in modern surgery, the removal of a muscle or bone has permanent consequences, that completely change a child's life. Likewise, irradiation of developing bone and muscle yields permanent effects. Usually, the younger the child, the more severe the late effects of therapy. It is important to understand the causes and the rehabilitation of limb length discrepancies, amputation, scoliosis, and other complications of therapy. Therapy is often more successful if the consequences are correctly anticipated and prevented, rather than waiting for deficits to develop.

Therapy can cause permanent deficits in the developing breast and skin. These may not appear at first to be as devastating as musculoskeletal late effects, but they may be much more severe than appreciated by the treating physicians and other members of the team.

In addition to the physical consequences, it is necessary to anticipate the psychological and social consequences, so that the child can understand the changes in his or her life. Treating the child and curing the cancer is not enough; understanding and dealing with the long-term consequences of treatment is critical as well.
16.2 Musculoskeletal

16.2.1 Pathophysiology

16.2.1.1 Normal Organ Development

The musculoskeletal system develops from the mesoderm and the neural crest. The mesoderm forms a series of tissue blocks on each side of the neural tube, which differentiate into the sclerotome (ventromedially) and the dermomyotome (dorsolateral). By the end of the fourth week of gestation, the sclerotome cells form a loose tissue called the mesenchyme, which then migrates and differentiates into fibroblasts, chondroblasts, and osteoblasts [63]. Cells from the myotome region of the dermomyotomes become elongated, spindle-shaped cells called myoblasts. These embryonic muscle cells fuse to form multinucleated muscle cells called muscle fibers. The dermatome regions of the dermomyotomes give rise to the dermis of the skin [38].

In the flat bones of the skull and face the mesenchyme develops directly into bone (membranous ossification); however, most of the remainder of the skeleton first forms hyaline cartilage, which in turn ossifies (endochondral ossification). Most of the ossification in the long bones occurs during fetal life.

The axial skeleton consists of the skull, the vertebrae, the sternum, and the ribs. The bones of the limbs make up the appendicular skeleton. The bones of the axial skeleton are flat or irregularly shaped. Most of the bones of the appendicular skeleton are long bones (see Fig. 16.1) [64] and have a shaft (diaphysis), a medullary cavity and two enlarged ends (epiphyses). The epiphysis at each end extends from the articular cartilage to the epiphyseal growth plate. The metaphysis is the region between the epiphyseal plate and the diaphysis. After initial ossification in utero, longitudinal growth of the bone occurs only at the epiphyseal plate (physiis). The mechanism of growth at the physiis is the proliferation of a layer of chondroblasts, which in turn form a layer of cartilage (Fig. 16.2). Small blood vessels invade the cartilage, increasing oxygen tension and stimulating the formation of osteoblasts. The osteoblasts create osteoid that calcifies into bone [60, 61].

Most skeletal muscle also develops before birth, although some muscle formation continues until the end of the first year of life. No new muscle cells are created after that time; muscle tissue enlarges due to increases in the number of myofilaments within each fiber, which result in an increase in the diameter of the individual muscle cells.

16.2.1.2 Organ Damage Induced by Cytotoxic Therapy

Direct damage to the developing musculoskeletal system from cytotoxic therapy is most often caused by irradiation. The cells most sensitive to irradiation