

dysfunction can occur acutely with symptoms of heart failure noted soon after drug administration, but more often is detected by surveillance echocardiography during the first year after exposure. Doxorubicin cardiotoxicity generally does not result in marked left ventricular dilation, such that stroke volume and systemic perfusion can be severely reduced with only a modest reduction of ejection fraction. Therapy for reduced ejection fraction includes β -adrenergic receptor blockade and inhibition of the renin-angiotensin system, with conflicting data on whether these agents decrease toxicity when given in parallel with chemotherapy. Once thought to have an inexorable downward course, many patients with symptomatic heart failure can improve to near-normal function with careful management, including prevention of “second-hit” insults such as atrial fibrillation or hypertension. The course differs for some children treated with these agents before puberty, in whom inadequate growth of the heart may lead to refractory heart failure as they reach their twenties.

Trastuzumab (Herceptin) is one of the humanized monoclonal antibodies that interfere with human epidermal growth receptor 2 (HER2), which is crucial for growth of some tumors, such as breast cancer, and for cardiac adaptation. Cardiotoxicity is highest when anthracyclines are administered in conjunction with trastuzumab; however, less toxicity is seen now when these agents are combined compared with the toxicity observed previously with paclitaxel for breast cancer. Although more often reversible than anthracycline cardiotoxicity, trastuzumab cardiomyopathy may persist in about a third of affected patients and can progress to clinical heart failure and death. For cardiotoxicity with anthracyclines or trastuzumab, therapy is recommended as for other causes of reduced ejection fraction, but it is not clear whether treatment enhances the spontaneous rate of improvement or whether it decreases progression.

Cardiotoxicity with *cyclophosphamide* and *ifosfamide* generally occurs acutely and with very high doses. 5-Fluorouracil, cisplatin, and some other alkylating agents can cause recurrent coronary spasm that occasionally leads to depressed contractility. Acute administration of *interferon- α* , interleukin 2, and other cytokine-based