menopause. Because the magnitude and extent of decreased fertility can be difficult to predict, patients should be counseled to maintain effective contraception, preferably by barrier means, during and after therapy. Resumption of efforts to conceive should be considered in the context of the patient's likely prognosis. Hormone replacement therapy should be undertaken in women who do not have a hormonally responsive tumor. For patients who have had a hormone-sensitive tumor primarily treated by a local modality, conventional practice would counsel against hormone replacement, but this issue is under investigation.

Chemotherapy agents have variable effects on the success of pregnancy. All agents tend to have increased risk of adverse outcomes when administered during the first trimester, and strategies to delay chemotherapy, if possible, until after this milestone should be considered if the pregnancy is to continue to term. Patients in their second or third trimester can be treated with most regimens for the common neoplasms afflicting women in their childbearing years, with the exception of antimetabolites, particularly antifolates, which have notable teratogenic or fetotoxic effects throughout pregnancy. The need for anticancer chemotherapy per se is infrequently a clear basis to recommend termination of a concurrent pregnancy, although each treatment strategy in this circumstance must be tailored to the individual needs of the patient.

SPECIAL ISSUES WITH TARGETED TREATMENTS

Treatment with EGFR-directed small molecules (e.g., erlotinib, afatinib, lapatinib), antibodies (e.g., cetuximab, panitumumab), and mTOR antagonists (e.g., everolimus, temsirolimus) reliably produces an acneiform rash that can be a source of distress to patients and can be ameliorated with topically applied clindamycin gels and low-potency corticosteroid creams. Diarrhea frequently accompanies tyrosine kinase inhibitor administration and may respond to antimotility agents such as loperamide or stool-bulking agents.

Anti-VEGFR-directed treatments, including the specific antibody bevacizumab, and the "multikinase" inhibitors with anti VEGFR activity, such as sorafenib, sunitinib, and pazopanib, reliably produce hypertension in a significant fraction of patients that typically can be treated with lisinopril, amlodipine, or clonidine alone or in combination. More difficult to treat is proteinuria with resultant azotemia; this can be a basis for discontinuing treatment depending on the clinical context. Thyroid function is prominently affected by chronic exposure to this group of multikinase inhibitors including sorafenib and pazopanib, and periodic surveillance of thyroid-stimulating hormone and thyroxine (T_4) levels during treatment is reasonable. Gastrointestinal perforations, arterial thromboses, and hemorrhage likewise have no specific treatments and may be a basis to avoid this class of agents. Palmar-plantar dysesthesia ("hand-foot syndrome") can be seen after administration of these agents (as well as some cytotoxic agents including gemcitabine and liposomal preparations of doxorubicin) and is a basis for considering dose reduction if not responsive to topical emollients and analgesics.

Protein kinase antagonists as a class have been associated with poorly predicted hepatic and cardiac toxicities (imatinib, dasatinib, sorafenib, pazopanib) or cardiac conduction deficits including prolonged QT interval (pazopanib). The occurrence of new cardiac or liver abnormalities in a patient receiving treatment with a protein kinase antagonist should lead to a consideration of the risk versus benefit and the possible relation of the agent to the new adverse event. The existence of prior cardiac dysfunction is a relative contraindication to the use of certain targeted therapies (e.g., trastuzumab), although each patient's needs should be individualized. **Chronic effects of cancer treatment are reviewed in Chap. 125.**