measure due to the relative rarity of cancer in children and the long duration of follow-up that might credibly be needed to see the effect. The inconsistent results and small effect sizes observed from diagnostic exposures make it likely that, if there is an effect, it is very small and, if there is not a significant effect, it will be impossible to prove that fact to everyone's satisfaction. No imaging using ionizing radiation should be done without a compelling reason and due consideration to obtaining the necessary information by other imaging modalities. Exposure to diagnostic and therapeutic radionuclides, especially radioactive iodine, poses unique risks, but a full discussion of these is beyond the scope of this chapter. Radiation therapy uses radiation doses three orders of magnitude greater than diagnostic procedures, entails substantial risks if the fetus is in the radiation field, and is rarely appropriate in pregnancy. Finally, although difficult to prove, it is likely that more harm has come to pregnant women from failing to perform appropriate diagnostic procedures than has been done to their offspring from performing appropriate diagnostic procedures.

CHEMOTHERAPY IN PREGNANCY

There are a number of reasons why it is impossible to make many definitive statements regarding the safety and efficacy of chemotherapy in pregnancy. All of the available data in the literature are published as case reports or case series. The quality and completeness of the data are inconsistent and often poor. Reports may come from medical oncologists, obstetricians, pediatricians, or other treating physicians familiar with the information important to the report from their own perspective but missing information important for other specialty areas. Reports frequently lack critical details of drug administration, such as dose, duration, cumulative dose, and timing of exposure in gestation, and outcomes, including birth weight and gestational age at delivery, indication for or cause of premature delivery, and follow-up of offspring beyond the immediate neonatal period. There are a wide variety of agents available to treat cancer, and they are usually used in combinations. This results in the fact that every patient is almost unique (an experiment of one) in the combination of agents, doses, durations, and gestational ages of administration, making it very difficult to attribute what benefit or toxicity accrues to which agent. Fortunately, cancer in pregnant women is sufficiently rare that it takes quite a while to accumulate enough information for any one agent or combination of agents to be confident about what toxicities (including congenital malformations) are truly associated with which agents. There is such rapid progress in cancer chemotherapy that by the time there may seem to be enough information about the agents currently in use to use them intelligently and counsel patients meaningfully, the cancer community has moved on to newer, more efficacious, and hopefully less toxic agents for which there is little or no experience in pregnancy. Finally, for obvious reasons, there are no untreated controls for comparison. It may be very difficult to sort out the maternal consequences (nausea, vomiting, fever, weight loss, dehydration) that might result directly from the malignancy and cause adverse pregnancy outcomes from some of the toxicities of the chemotherapeutic agents used to treat the malignancy.

Generally, toxic chemotherapy should be avoided during pregnancy, if at all possible. It should virtually never be given in the first trimester. However, a variety of single agents and combinations have been given in the second and third trimesters, without a high frequency of toxic effects to the pregnancy or the fetus, but data on safety are sparse. Maternal factors that may influence the pharmacology of chemotherapeutic agents include the 50% increase in plasma volume, altered absorption and protein binding, increased glomerular filtration rate, increased hepatic mixed function oxidase activity, and third space created by amniotic fluid. The fetus is protected from some agents by placental expression of drug efflux pumps, but decreased fetal hepatic mixed function oxidase and glucuronidation activity may prolong the half-life of agents that do cross the placenta. A database on the risks associated with individual chemotherapy agents is available on the Internet (*http://ntp.niehs.nih.gov/ntp/ohat/cancer_chemo_preg/chemopregnancy_monofinal_508.pdf*).

Optimal management strategies have not been developed based on prospective clinical trials. Management of a malignancy complicating pregnancy will be critically determined by the gestational age when the malignancy is diagnosed and the anticipated natural history of the lesion, if left untreated. On one extreme, if the malignancy is slowly progressive, the patient is near her delivery date, and waiting until delivery to begin treatment would not be anticipated to compromise maternal prognosis, then treatment could be delayed until after delivery to avoid fetal exposure to chemotherapy. If there is a greater sense of urgency to begin definitive treatment to avoid compromising maternal prognosis, and the patient is beyond 24 weeks of gestation but remote from her delivery date, then treatment (surgical, medical, or both) might be initiated during pregnancy and plans made to deliver the fetus early to avoid exposure to more chemotherapy than absolutely necessary. Finally, if the patient is in her first trimester and toxic chemotherapy must be initiated promptly to avoid a very poor maternal outcome, then it may be necessary to consider therapeutic abortion to avoid maternal disaster and fetal survival with injury resulting in long-term morbid sequelae. No two cases are precisely alike, and inevitably, decision making must be individualized, preferably with consultation with a multidisciplinary team including medical oncology, surgical oncology if appropriate, maternal–fetal medicine, neonatology, and anesthesia. Pregnancy appears to have little or no impact on the natural history of malignancies, despite the hormonal influences. Spread of the mother's cancer to the fetus (so-called *vertical transmission*) is exceedingly rare.

CERVICAL CANCER DURING PREGNANCY

The incidence of cervical cancer in pregnant women is roughly comparable to that of age-matched controls who are not pregnant. Invasive cervical cancer complicates about 0.45 in 1000 live births, and carcinoma in situ is seen in 1 in 750 pregnancies. About 1% of women diagnosed with cervical cancer are pregnant at the time of diagnosis. Early signs of cervical cancer include vaginal spotting or discharge, pain, and postcoital bleeding, which are also common features of pregnancy. Early visual changes in the cervix related to invasive cancer can be mistaken for cervical decidualization or ectropion (columnar epithelium on the cervix) due to pregnancy. Women diagnosed with cervical cancer during pregnancy report having had symptoms for 4.5 months on average.

Approximately 95% of all cervical cancer is caused by human papillomavirus (HPV) infections, with types 16 and 18 accounting for about 70% of cervical cancer. The rate of carriage of these serotypes is highest among women in their early twenties and can be reduced with the use of vaccination before exposure. Women generally tend to clear the infection by age 30, with the risk of cervical cancer being highest among those who fail to clear the infection. Screening is recommended at the first prenatal visit and 6 weeks postpartum. The rate of cytologic abnormalities on Pap smear in pregnant women is about 5–8% and is not much different than the rate in nonpregnant women of the same age.

In 2012, several sets of recommendations were published for screening for cervical cancer: one by the American Cancer Society (ACS), the American Society for Colposcopy and Cervical Pathology (ASCCP), and the American Society for Clinical Pathology (ASCP); a second by the U.S. Preventive Services Task Force (USPSTF); and a third by the American College of Obstetricians and Gynecologists (ACOG). Although the details of the recommendations for screening and management of abnormal results differ slightly among the three sets of guidelines, there is general consensus that cytology screening should start at age 21 and continue every 3 years through age 29. After age 30, cytology screening frequency may be reduced to every 5 years if accompanied by co-testing for HPV. Recommendations for management of abnormal cytology findings are complex and determined by the degree of abnormality of the cytology finding (e.g., atypical squamous cells of undetermined significance; atypical squamous cells, cannot exclude high-grade squamous intraepithelial lesion; low-grade squamous intraepithelial lesion; or high-grade squamous intraepithelial