high-risk populations showed that ultrasound was more sensitive than AFP elevations alone, although most practitioners request both tests at 6-month intervals for HBV and HCV carriers, especially in the presence of cirrhosis or worsening of liver function tests. However, an Italian study in patients with cirrhosis identified a yearly HCC incidence of 3% but showed no increase in the rate of detection of potentially curable tumors with aggressive screening. Prevention strategies including universal vaccination against hepatitis are more likely to be effective than screening efforts. Despite absence of formal guidelines, most practitioners obtain 6-month AFP and ultrasound (cheap and ubiquitous, even in poor countries) or CT (more sensitive, especially in overweight patients, but more costly) studies when following high-risk patients (HBV carriers, HCV cirrhosis, family history of HCC).

Current Directions Cost-benefit analysis is not yet convincing, even though screening is intuitively sound. However, studies from areas with high HBV carrier rates have shown a survival benefit for screening as a result of earlier stage at diagnosis. A definitive clinical trial on screening is unlikely, due to difficulties in obtaining informed consent for patients who are not to be screened. γ-Glutamyl transpeptidase appears useful for detecting small tumors.

PREVENTION

Prevention strategies can only be planned when the causes of a cancer are known or strongly suspected. This is true of few human cancers, with significant exceptions being smoking and lung cancer, papilloma virus and cancer of the cervix uteri, and cirrhosis of any cause or dietary contamination by aflatoxin B_1 for HCC. Aflatoxin B_1 is one of the most potent known chemical carcinogens and is a product of the *Aspergillus* mold that grows on peanuts and rice when stored in hot and humid climates. The obvious strategy is to refrigerate these foodstuffs when stored and to conduct surveillance programs for elevated aflatoxin B_1 levels, as happens in the United States, but not usually in Asia. HBV is commonly transmitted from mother to fetus in Asia (except Japan), and neonatal HBV vaccination programs have resulted in a big decrease in adolescent HBV and, thus, in predicted HCC rates. There are millions of HBV and HCV carriers (4 million with HCV in the United States) who are already infected. Nucleoside analogue–based chemoprevention (entecavir) of HBV-mediated HCC in Japan resulted in a fivefold decrease in HCC incidence over 5 years in cirrhotic but not in noncirrhotic HBV patients. More powerful and effective HCV therapies promise the possibility of prevention of HCV-based HCC in the future.

TREATMENT HEPATOCELLULAR CARCINOMA

Most HCC patients have two liver diseases, cirrhosis and HCC, each of which is an independent cause of death. The presence of cirrhosis usually places constraints on resection surgery, ablative therapies, and chemotherapy. Thus patient assessment and treatment planning have to take the severity of the nonmalignant liver disease into account. The clinical management choices for HCC can be complex **(Fig. 111-2, Tables 111-5 and 111-6)**. The natural history of HCC is highly variable. Patients presenting with advanced tumors (vascular invasion, symptoms, extrahepatic spread) have a median survival of ~4 months, with or without treatment. Treatment results from the literature are difficult to interpret. Survival is not always a measure of the efficacy of therapy because of the adverse effects on survival of the underlying liver disease. A multidisciplinary team, including a hepatologist, interventional radiologist, surgical oncologist, resection surgeon, transplant surgeon, and medical oncologist, is important for the comprehensive management of HCC patients.

TNM STAGES I AND II HCC

Early-stage tumors are successfully treated using various techniques, including surgical resection, local ablation (thermal, radiofrequency [RFA], or microwave ablation (MWA]), and local injection therapies (Table 111-6). Because the majority of patients with HCC suffer from a field defect in the cirrhotic liver, they are at risk for subsequent multiple primary liver tumors. Many will also have significant underlying liver disease and may not tolerate major surgical loss of hepatic parenchyma, and they may be eligible for orthotopic liver transplant (OLTX). Living related donor transplants have increased in popularity, resulting in absence of waiting for a transplant. An important principle in treating early-stage HCC in the nontransplant

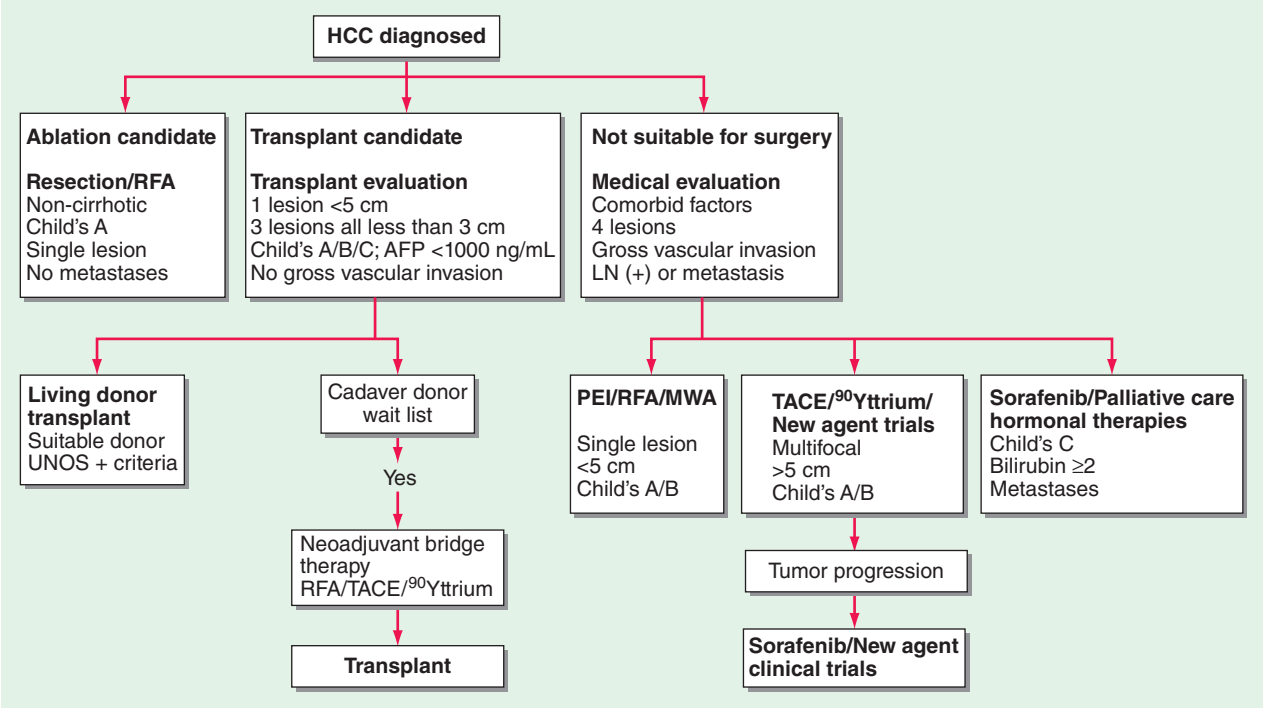

FIGURE 111-2 Hepatocellular carcinoma (HCC) treatment algorithm. The initial clinical evaluation is aimed at assessing the extent of the tumor and the underlying functional compromise of the liver by cirrhosis. Patients are classified as having resectable disease or unresectable disease or as being candidates for transplantation. AFP, α fetoprotein; LN, lymph node; MWA, microwave ablation; OLTX, orthotopic liver transplantation; PEI, percutaneous ethanol injection; RFA, radiofrequency ablation; TACE, transcatheter arterial chemoembolization; UNOS, United Network for Organ Sharing. Child's A/B/C refers to the Child-Pugh classification of liver failure.