Therapeutic concepts in hepatocellular carcinoma and bile duct carcinoma are undergoing considerable change. Technologic advances have stimulated the use of investigational approaches including resection, embolization, intra-arterial cytotoxic therapy, radiation, and a combination of these, as well as the trial of new and standard drugs or combination regimens by the systemic route. Pharmacologic studies are becoming more frequent and are essential for the proper evaluation. The interpretation of results is difficult because of the paucity of information on natural history or any large series of adequately staged and similarly treated patients. In the review of data on single drugs, it should be kept in mind that there is often inadequate therapeutic information and an inadequate description of prognostic factors. Data on bile duct carcinoma are not available beyond some small experience with 5-fluorouracil (5-FU) or 5-FU combinations [1,2,3, and chapter 15].

BACKGROUND
Liver cancer is primarily of the hepatocellular type in the United States, with less than 10% being defined histologically as cholangiocarcinoma or other rarer pat-
terns [4 and chapter 1]. In the majority of instances the tumor is localized to the liver at presentation, but this factor does not preclude early termination in hepatic failure, or a very low resectability rate. Nevertheless it does encourage regional approaches directed at the eradication of tumor confined to the liver, resulting in an increased interest in combinations of local therapies and drugs, or infusion of drugs via the hepatic artery. Other noteworthy features include the presence of very vascular tumors and prior infection with hepatitis B, and the consequences such as postnecrotic cirrhosis and transplacental infections. In addition, certain hepatocellular carcinomas are associated with production of alpha-fetoprotein (AFP) and occasionally other tumor manifestations such as dysfibrinogenemia. Male predominance is typical.

Various classifications have been utilized in order to establish prognostic categories (see chapter 1). Grossly the tumor presents as a nodular (multiple discrete nodules), a massive (a large predominant mass with satellites), or a diffuse form (indistinct minute nodules common in cirrhosis). Microscopic classifications include a spectrum from well-differentiated tumors to highly undifferentiated ones.

Metastases occur most frequently in peripheral lymph nodes and lung, and less frequently in bones, adrenals, and brain. Massive hemorrhage into the peritoneal cavity occurs occasionally, as does thrombosis of portal or hepatic veins.

Information about bile duct carcinomas and their systemic therapy is scanty. Radical surgery has curative potential in tumors of the distal common duct. As discussed by Ottow (chapter 6), surgery offers the only chance for cure. Unfortunately, few patients with these disease are candidates for a curative procedure. Surgery does, however, have a definite role in the palliative management of these patients and may provide some degree of relief from pain and jaundice. Except for a limited experience with the fluoropyrimidines and anthracyclines, no substantial data are available on the efficacy of other agents [1,4,5, and chapter 15]. When resection cannot be performed, radiation and 5-FU have been utilized with disappointingly short responses (chapter 18).

PROGNOSTIC FACTORS

The first two chapters have reviewed pathologic and clinical factors which may have an impact on prognosis and response to treatment. Other demographic factors such as age and ethnic origin may also have prognostic implication. We briefly describe them so that they may be considered in the design and reporting of Phase II and III trials.

One gross pathologic classification referred to above includes the massive, nodular, and diffuse types [6]. Microscopic classifications include trabecular, pseudoglandular, solid (anaplastic), pelioid, clear cell, and fibrolamellar types. The latter two have a better prognosis [7,8,9].

Functional and anatomic stages were proposed by Vogel and Linsell [7] and subsequently utilized by Primack and others to describe results of their trials performed in Uganda in the 1970s [8]. Following these clinical trials, adoption of description by Child's functional stage (i.e., no or minimal liver decompensation