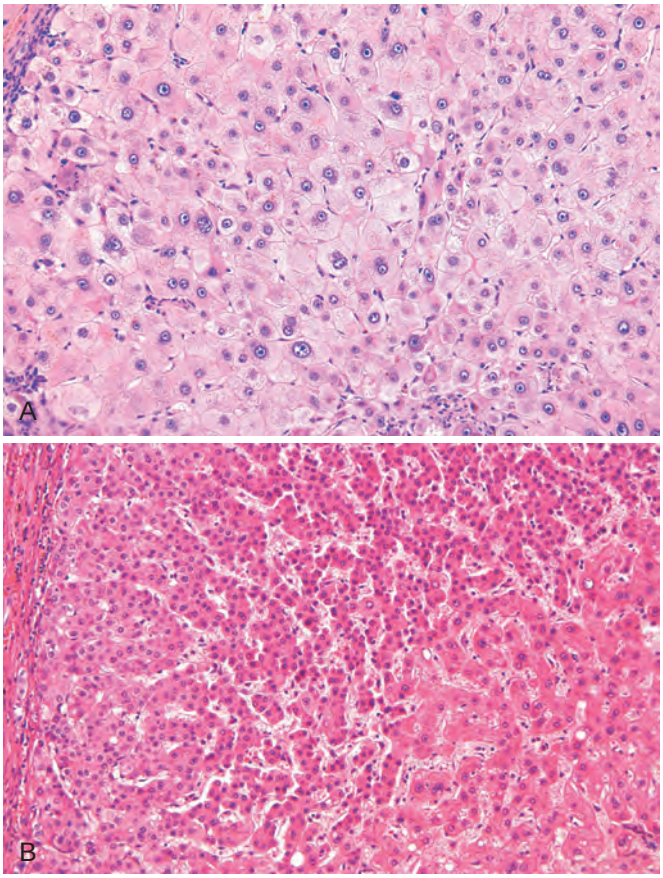

Figure 18-57 **A,** Large cell change. Large hepatocytes with large, often atypical nuclei are scattered among normal-size hepatocytes with round, typical nuclei. **B,** Small cell change. The abnormal cells have a high nuclear-to-cytoplasmic ratio and are separated by thickened plates. Normal-appearing hepatocytes are in the lower right corner. (Courtesy Dr. Young Nyun Park, Yonsei Medical College, Seoul, South Korea.)

undergo transformation to higher grade lesions, but they at least indicate a higher risk for HCC in the liver as a whole. *High-grade dysplastic nodules* are probably the most important primary pathway for emergence of HCC in viral hepatitis and alcoholic liver disease. Subnodules of HCC are often found in high-grade dysplastic nodules in biopsy or resection specimens.

MORPHOLOGY

Large cell change shows scattered hepatocytes, usually near portal tracts or septa, that are larger than normal hepatocytes and with large, often multiple, often moderately pleomorphic nuclei; however, the nuclear-cytoplasmic ratio is normal since both nuclei and the cell as a whole become larger (Fig. 18-57*A*). In **small cell change** the hepatocytes have high nuclear-cytoplasmic ratio and mild nuclear hyperchromasia and/or pleomorphism (Fig. 18-57*B*). Hepatocytes exhibiting small cell change often form tiny expansile nodules within a single parenchymal lobule.

Low-grade dysplastic nodules are devoid of cytologic or architectural atypia, but have been shown to be clonal and are probably neoplastic, rather than simply large cirrhotic nodules. Portal tracts are still present within these nodules, often in near normal distribution. Thus, the blood supply remains a mix of portal venous and hepatic arterial blood. **High grade dysplastic nodules** have cytologic (e.g., small cell change) or architectural features (occasional pseudoglands, trabecular thickening) suggestive of, but still insufficient for diagnosis of overt HCC. Such atypia often presents as a subnodule within the larger nodule. Portal tracts are fewer in these higher grade nodules and arteries feeding the growing lesion gradually come to predominate over the portal veinous flow. Overt HCC may then arise within the dysplastic nodules (Fig. 18-58*B*), eventually overgrowing it.

Overall, **HCC may appear grossly as (1) a unifocal (usually large) mass, (2) multifocal, widely distributed nodules of variable size, or (3) a diffusely infiltrative**

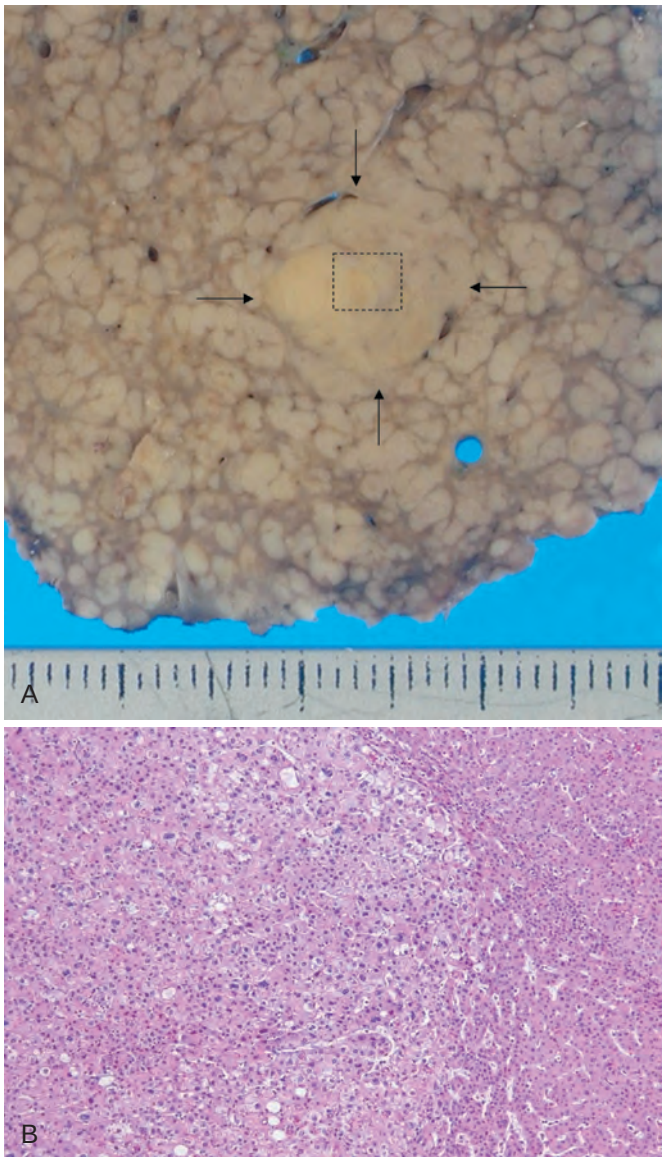

Figure 18-58 **A,** Hepatitis C–related cirrhosis with a distinctively large nodule *(arrows).* Nodule-in-nodule growth suggests an evolving cancer. **B,** Histologically the region with in the box in **A** shows a well-differentiated hepatocellular carcinoma (HCC) (right side) and a subnodule of moderately differentiated HCC within it (center, left). (Courtesy Dr. Masamichi Kojiro, Kurume University, Kurume, Japan.)