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CURRENT PEDIATRIC THERAPY

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measures, sclerosing injections or portal shunting may become necessary in many survivors.

Ascites. A combination of hypoalbuminemia, hyperaldosteronism, and renal failure associated with impairment of liver function may result in retention of sodium and total body water, whereas portal hypertension appears to be mainly responsible for the localization of excess fluid in the abdomen. Sudden ascites can be precipitated during the course of chronic liver disease by intercurrent infections, hemorrhage, or surgery. Acute ascites is often reversed by limiting daily dietary sodium to 500 mg. Children on this diet should receive an adequate caloric and protein intake.

"Chronic" ascites, which is a reflection of progressive liver decompensation and portal hypertension, gradually results in discomfort, dyspnea, and severe limitation of physical activity. In addition to dietary management, successful diuresis in these patients may be accomplished with the combinations of diuretic agents and inhibitors of sodium-potassium exchange.

Treatment is initiated in the hospital. A dietitian prescribes salt-depleted proteins and starches to augment caloric intake and to make the diet more palatable and adds vitamin supplements. In children with advanced cirrhosis, protein intake is limited to 1 gm/kg/day because of the danger of hepatic coma. The most useful diuretic is spironolactone, 3 mg/kg/day. Dosages may be decreased or increased according to the diuretic response. A mean 24-hour weight loss of up to 1 pound is considered satisfactory. Serum sodium and potassium levels should be determined daily, especially during the initial stages of therapy. Spironolactone usually obviates the need for potassium supplements. Chlorothiazide (30 mg/kg/day) in combinations with spironolactone up to 7 mg/kg/day often controls refractory ascites. Furosemide, 2 mg/kg/dose, is reserved for the most resistant cases.

Coma. Coma can be precipitated in a cirrhotic patient by infection, fluid imbalance, diuretic therapy, hemorrhage, and surgery. Appropriate respective measures include antibiotics, correction of over- or underhydration, removal of diuretics, prevention of hemorrhage and, obviously, avoidance of surgery. Current therapy of hepatic coma is based on efforts to diminish ammonia by eliminating protein intake during the comatose period and using poorly absorbed antibiotics, such as neomycin, kanamycin, or paromomycin, to control intestinal ammonia-producing bacteria. A daily oral dose of neomycin, 2 to 4 gm, is given during the acute periods; smaller doses may be required for maintenance. Lactulose, 60 gm/day in 3 doses, is also effective in control of ammonia. This non-absorbable sugar acts as substrate for acid production by colonic flora, resulting in flux of ammonia from the circulation to the intestinal lumen. Other

measures include control of renal ammonia by maintenance of normal potassium levels and avoidance of diuretics.

Patients with uncomplicated chronic liver disease usually recover when treated in this manner, but those with progressive liver disease usually do not. Liver transplantation may offer a chance for survival in such patients.

Tumors of the Liver

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MALIGNANT TUMORS

Mass lesions of the liver diagnosed by radiologic studies should be considered malignant until proved otherwise. The most common malignant tumor in children is hepatoblastoma. Hepatocellular carcinoma is the second most common and usually occurs in older children. Sarcomas of the liver, such as rhabdomyosarcoma and angiosarcoma, are rare. None of these has a favorable outlook, but fibrolamellar hepatocellular carcinoma, which is common in older children and young adults, has a better prognosis than other types of liver malignancy.

The treatment for all malignant liver tumors is complete surgical excision by anatomic hepatic resection. Hepatic resections of more than the right or left lobe of the liver can be performed quite safely. For example, a large tumor occupying the right lobe and the medial segment of the left lobe can be resected by right hepatic trisegmentectomy, leaving only the left lateral segment of the left lobe (to the left of the falciform ligament); or a large tumor occupying the left lobe and anterior segment of the right lobe can be resected by left hepatic trisegmentectomy, leaving only the posterior segment of the right lobe. These extensive right and left hepatic trisegmentectomies can now be performed by experienced surgeons with less than a 5% operative mortality.

We have found that computed tomography is most useful to assess the extent of the tumor, but it can be often misleading, particularly when a large tumor distorts normal anatomic boundaries. If resectability is uncertain after extensive preoperative investigations, the patient should be referred to a surgeon who is experienced in major hepatic resections rather than submitted to exploratory celiotomy by someone who is unprepared to undertake a definitive procedure.

After curative hepatic resections, we often recommend that patients receive adjuvant chemotherapy for at least a year. We have been using combination chemotherapy with doxorubicin, dacarbazine, vincristine, cyclophosphamide, and

often mitomycin. The value of this approach has not been validated in randomized trials, but the patients who have received adjuvant chemotherapy have seemed to live longer, tumor-free.

Liver transplantation is an ineffective cancer therapy at this time. We have treated 50 patients with various primary liver malignancies by orthotopic liver transplantation (total hepatectomy and liver replacement). Nearly all the patients who received liver replacement for the treatment of nonresectable large malignant tumors developed tumor recurrences, with the exception of those with fibrolamellar hepatomas. Fibrolamellar hepatocellular carcinoma seemed to carry a better prognosis after liver replacement, just as after partial liver resection. On the other hand, most of the patients who have received liver replacement primarily for other end-stage liver diseases, such as tyrosinemia and α_1 -antitrypsin deficiency disease, and whose malignant liver tumors were small and incidental, survived tumor-free for several years.

The most common metastatic liver tumors in children are neuroblastoma and Wilms' tumor. Although chemotherapy and radiation therapy may be helpful in treating these metastatic tumors, the lesion should be excised whenever possible, particularly if it is localized to part of the liver. We have performed nearly 100 liver resections for metastatic liver tumors without any operative mortality.

BENIGN TUMORS

Most of the benign tumors of the liver are asymptomatic and are found incidentally during studies for other disorders or during abdominal operations.

Hemangiomas are the most common benign tumors of the liver. Giant cavernous hemangiomas should be treated by surgical excision, particularly if they are symptomatic. The majority of giant cavernous hemangiomas require lobectomies or trisegmentectomies of the liver, but some, which are located on the surface of the liver or which are pedunculated, can be enucleated along pseudocapsular margins without significant loss of normal liver tissue.

Infantile hemangioendotheliomas are most often seen in infants during the first 6 months of life and are distinct from cavernous hemangiomas. The lesions should be excised by anatomic hepatic resection whenever possible. If the patient's condition prohibits surgery, treatment with prednisone, diuretics, and digoxin can be used initially. Response to prednisone may allow surgery to be performed safely in 2 weeks. In extensive lesions, radiation to the liver may be used after pathologic diagnosis is confirmed by open liver biopsy. Favorable responses to steroids, radiation, and he-

patic artery ligation or embolization have been reported. The treatment should be vigorous, because complete regression and cure are possible.

Other benign tumors include adenoma, hamartoma, focal nodular hyperplasia, fibroma, and teratoma. Radiologic differentiation of these benign tumors from malignant tumors is unreliable. Pathologic confirmation of benign tumor is mandatory for each lesion. Large benign tumors should be treated by surgical excision, particularly if they are symptomatic. Adenoma has a tendency to rupture and cause life-threatening hemorrhage. Some adenomas cannot be easily differentiated from low-grade hepatocellular carcinoma by needle biopsies. If the diagnosis is uncertain, the lesion should be excised with an adequate margin without delay.

Portal Hypertension

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Portal hypertension is nearly always due to obstruction to blood flow in the portal venous system. It can be divided into two main categories: pre-sinusoidal, and sinusoidal or postsinusoidal. It is important to make the distinction. In the pre-sinusoidal type of portal hypertension, hepatocellular function is intact, whereas in the second form it is defective, and liver cell failure is liable to be precipitated by hemorrhage. Treatment depends upon accurate localization of the site of obstruction and, if possible, knowledge of the cause.

Management Before and Between Hemorrhages. Apart from any treatment necessary for underlying cirrhosis, the child should be allowed to lead as normal a life as possible and attend ordinary school. Provided the spleen is not too large, games and physical education may be allowed. Particularly vigorous sports, such as football, must be forbidden. The child should not be allowed to become overly tired. The school principal should be informed of the situation, and the parents should not press the child to be too competitive in either work or play.

Note should be taken of fecal color and the parents told to report if it becomes black. Hemoglobin estimations should be done if the child appears anemic or passes black stools. Oral iron treatment is given as required. The cirrhotic child requires occasional estimations of the prothrombin time, and intramuscular vitamin K₁ (5 mg) may be useful from time to time.

Hemorrhage commonly follows an upper respiratory tract infection, and this should be avoided if possible and all necessary inoculations given. If infection develops, it should be taken seriously and broad-spectrum antibiotics given from the