Personal Experience With 411 Hepatic Resections

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Over a 24-year period, 411 partial hepatic resections were performed: 142 right or left trisegmentectomies, 158 lobectomies, 25 segmentectomies, and 86 local excisions. The operations were performed for benign lesions in 182 patients, for primary hepatic malignancies in 106, and for hepatic metastases in 123, including 90 from colorectal cancers. The 30-day (operative) mortality rate was 3.2%, and there were an additional six late deaths (1.5%) due to hepatic failure caused by the resection. The highest operative mortality rate (6.3%) resulted from the trisegmentectomies, but this merely reflected the extent of the disease being treated. A mortality rate of 8.5% for patients with primary hepatic malignancy was associated not only with the extensiveness of lesions, but also with cirrhosis in the remaining liver fragment. There was no mortality for 123 patients with metastatic disease, 100 patients with cavernous hemangioma, 22 with liver cell adenoma, 17 with focal nodular hyperplasia, 16 with congenital cystic disease, and five with hydatid cysts. Trauma, pre-existing iatrogenic injury, and cirrhosis were the only conditions that had lethal portent in patients with benign disease. Furthermore, patients with benign disease who survived operation had minimal liability from recurrence of their original disease and none from the resection *per se*. By contrast, tumor recurrence dominated the actuarial survival rates for cancer patients, which at 1 and 5 years were 68.5% and 31.9%, respectively, after resection for primary hepatic malignancy, and 84.2% and 29.5%, respectively, for hepatic metastases. In this report, the expanding role of partial hepatectomy in the treatment of liver disease was emphasized, as well as the need for considering, in some cases, the alternative of total hepatectomy and liver replacement.

ALTHOUGH HEPATIC RESECTION was first carried out over a century ago,[1] it was not until the precise lobar and segmental anatomy of the liver was appreciated that controlled anatomic hepatic resection

became feasible.[2–7] Almost two more decades ensued before hepatic resections could be performed safely by many surgical specialists interested in this field.

Our interest in hepatic resection started with the referral of patients for liver transplantation whose hepatic lesions were believed to be too extensive for subtotal hepatectomy. Many such masses could be resected with modifications of previously described but uncommonly used operations, such as right trisegmentectomy,[8,9] or with operations not previously performed.[10] Portions of this experience have been reported earlier.[8–15]

Methods

Case Material

Four hundred eleven patients were treated consecutively at the University of Colorado Health Sciences Center (1964–1980) and at the University Health Center of Pittsburgh (1981–1987). The case load increased over the years (Table 1), 78 resections being carried out in 1987 alone.

The patients ranged in age from 11 months to 81 years. Twenty-five of the total 411 were younger than 18 years of age, and 22 were younger than 12 years of age. The 182 patients with benign hepatic lesions (Table 2) were operated on either because they had the appropriate symptoms or because malignancy could not be ruled out. Of the 229 malignant lesions, 106 were primary in the liver, and 123 were metastatic from various origins (Table 2).

Kinds of Resections

There were six categories of hepatic resections (Fig. 1): right and left trisegmentectomy, right and left lobectomy,

TABLE 1. *Incidence of Hepatic Resection by 5-year Period and Indication*

Years	Number of Patients	Benign Lesion	Primary Malignancy	Secondary Malignancy
1964–1970	6	4	2	0
1971–1975	25	10	10	5
1976–1980	77	32	17	28
1980–1985	181	87	43	51
1986–1987	122	49	34	39
Total	411	182	106	123

left lateral segmentectomy, and nonanatomical local resection. With right trisegmentectomy, the left posterior portion of the caudate lobe was removed or retained, depending upon the location of the tumor.[8] Similarly, with left trisegmentectomy, the caudate process alongside the retrohepatic vena cava was removed or spared, as dictated by the tumor location.[10] "Extended" left or right lobectomy, which removed only a portion of the anterior or medial segment, respectively, were considered left or right lobectomy.

Nonanatomical local excisions were used primarily to excise benign tumors or to remove malignant tumors in patients with high operative risk factors. Some of these so-called local excisions were those of huge lesions and

were more difficult than anatomic resections (Fig. 2). The kinds of hepatic resection used for benign and malignant hepatic lesions, as well as the operative mortalities, are summarized in Table 3.

Statistical Analysis

The results were summarized as of April 1, 1988 with a minimum follow-up of 3 months. The survival rates were calculated by the method of Kaplan-Meier, and statistical comparisons were made by the method of Breslow and of Mantel-Cox.

Results

Operative Mortality

Operative mortality, defined as death within 1 month of the operation, totaled 13 (3.2%) of 411 patients (Table 3). Nine (6.3%) of 142 patients submitted to right or left trisegmentectomy died, as well as three (1.9%) of 158 submitted to right or left lobectomy. One (0.9%) of the remaining 111 patients died after a nonanatomic resection (Table 3).

The mortality rate of patients who received treatment of primary hepatic malignancy was 8.5% (Table 3). There

TABLE 2. *Indications for 411 Hepatic Resections*

Benign Hepatic Lesion (182 Patients)		Primary Hepatic Malignancy (106 Patients)		Secondary Hepatic Malignancy (123 Patients)	
Lesion	No. of Pts.	Malignancy	No. of Pts.	Malignancy	No. of Pts.
Cavernous Hemangioma	100	Hepatocellular carcinoma (HCC)	67	Colorectal cancer	90
Adenoma	22	Fibrolamellar HCC	12	Intestinal cancer	6
FNH	17	Nonfibrolamellar	55	Carcinoid	4
Congenital cyst	16	Cholangiocarcinoma (CHC)	14	Spindle cell sarcoma	1
Polycystic disease	6	Bile duct cancer	6	Leiomyosarcoma	1
Nonpolycystic disease	10	Carcinoma of hepatic cyst wall	4	Kidney cancer	5
Trauma	10	Leiomyosarcoma	4	Renal cell cancer	3
Hydatid cyst	5	Rhabdomyosarcoma	2	Wilm's tumor	2
Abscess	4	Hepatoblastoma	2	Adrenal cancer	5
Caroli's Disease	2	Angiosarcoma	1	Adrenocortical carcinoma	4
Fibroma	1	Adenocarcinoma of gallbladder	1	Neuroblastoma	1
Leiomyoma	1	Sarcoma, undetermined cell type	1	Breast cancer	4
Mesenchymal Hamartoma	1	Neuroendocrine tumor	1	Adenocarcinoma	2
Mesenchymoma	1	Adenocarcinoma	1	Comedocarcinoma	1
Regenerative Nodule	1	Unclassified malignancy	2	Angiosarcoma	1
Organized Hematoma	1			Gastric leiomyosarcoma	2
				Ovarian adenocarcinoma	2
				Uterus cancer	2
				Squamous cell cancer	1
				Endometrial sarcoma	1
				Melanoma	2
				Glucagonoma, pancreas	1
				Leiomyosarcoma, rectum	1
				Thyroid medullary carcinoma	1
				Ewing's sarcoma	1
				Mesothelioma	1

was no mortality in resections for metastatic tumor. Four (2.2%) of 182 patients with benign hepatic lesions died.

Seventeen of the 411 patients had gross cirrhosis; five of these patients (29.4%) died. By contrast, the mortality rate of patients without gross cirrhosis was eight (2%) of 394 (p < 0.01). Four of the nine deaths after resections for primary hepatic malignancy were those of patients with obvious cirrhosis.

Causes of Death

Deaths Within 1 Month. Details of the 13 operative deaths are summarized in Table 4. There were six deaths in the operating room, four due to bleeding, one due to myocardial infarction, and one due to perforation of the atrium by a central venous catheter. Hemorrhage was inherently uncontrollable in two of the foregoing cases because the venous drainage of the remaining hepatic fragment was compromised by the tumor or the trauma that had led to the operation.

Four additional patients died or underwent an attempt at liver transplantation during the first week after resection (Table 4). Two of these four patients had cirrhosis and died of liver failure, whereas a third patient underwent liver transplantation 6 days after an unwise attempt at right trisegmentectomy had compromised the inferior vena cava just above the diaphragm. The death due to hepatic failure of one of these patients was particularly tragic because the "hepatoma" that had prompted a lobectomy had been a large regenerative nodule (pseudohepatoma). A fourth patient with blunt trauma died suddenly 1 day after operation. The only findings at autopsy were cardiomegaly and microscopic fat emboli in the heart and the lungs.

Three other patients died after 19, 20, and 29 days, respectively. The first of these patients was referred to us with a previously reported dissection of the coeliac axis caused by preoperative angiography,[9] and the second patient arrived at our institution with intrahepatic abscesses secondary to hepatic artery and hepatic duct injuries during cholecystectomy. The third patient died 29 days after right trisegmentectomy and left lateral segmental duct reconstruction for Klatskin tumor.

Another perspective is provided by correlating the data in Tables 3 and 4. Only two patients with benign disease died, and these were patients with traumatic injuries severe enough to require trisegmentectomy, the one patient having an iatrogenic liver abscess, and the other having cirrhosis and the regenerative nodule of whom was misdiagnosed. Of any of the patients who underwent resections, the highest mortality rate was that of patients who underwent trisegmentectomy (6.3%). Yet five of the nine deaths that occurred with trisegmentectomy resulted from the treatment of very extensive primary hepatic malig-
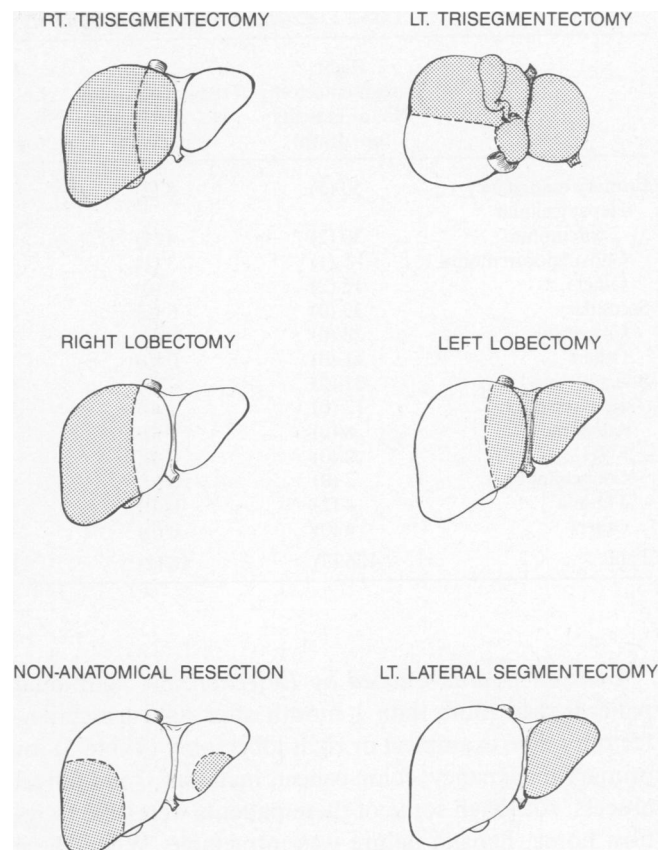

FIG. 1. Six categories of hepatic resections.

nancies, and two additional deaths occurred after the treatment of massive hepatic trauma. Excluding these high-risk cases, the mortality of trisegmentectomy would have been less than 2%.
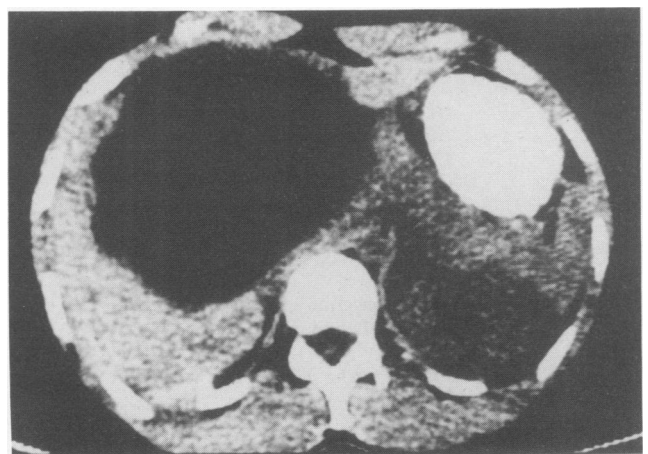

FIG. 2. Nonanatomical local excision of this huge congenital cyst resulted in prolonged bile leak, which ceased 1 month later without surgical intervention.

TABLE 3. *Extent of Hepatic Resections, Its Indication, and Operative Mortality (411 Patients)*

	Right Trisegmentectomy No. of Patients (op. death)	Left Trisegmentectomy No. of Patients (op. death)	Right Lobectomy No. of Patients (op. death)	Left Lobectomy No. of Patients (op. death)	Left Lateral Segmentectomy No. of Patients (op. death)	Local Excision No. of Patients (op. death)	Total No. of Patients (op. death)
Primary malignancy	50 (5)	8 (2)	17 (1)	18 (0)	4 (0)	9 (1)	106 (9)
Hepatocellular carcinoma	30 (2)	4 (1)	13 (1)	12 (0)	3 (0)	5 (1)	67 (5)
Cholangiocarcinoma	5 (1)	3 (1)	2 (0)	3 (0)	0 (0)	1 (0)	14 (2)
Others	15 (2)	1 (0)	2 (0)	3 (0)	1 (0)	3 (0)	25 (2)
Secondary	39 (0)	6 (0)	43 (0)	16 (0)	12 (0)	7 (0)	123 (0)
Colorectal	28 (0)	6 (0)	30 (0)	14 (0)	9 (0)	3 (0)	90 (0)
Others	11 (0)	0 (0)	13 (0)	2 (0)	3 (0)	4 (0)	33 (0)
Benign lesion	37 (2)	2 (0)	50 (2)	14 (0)	9 (0)	70 (0)	182 (4)
Hemangioma	12 (0)	1 (0)	26 (0)	5 (0)	6 (0)	50 (0)	100 (0)
Adenoma	8 (0)	1 (0)	8 (0)	3 (0)	0 (0)	2 (0)	22 (0)
FNH	2 (0)	0 (0)	3 (0)	1 (0)	1 (0)	10 (0)	17 (0)
Congenital Cyst	7 (0)	0 (0)	3 (0)	2 (0)	0 (0)	4 (0)	16 (0)
Trauma	4 (2)	0 (0)	4 (0)	1 (0)	1 (0)	(0) (0)	10 (2)
Others	4 (0)	0 (0)	6 (2)	2 (0)	1 (0)	4 (0)	17 (2)
Total	126 (7)	16 (2)	110 (3)	48 (0)	25 (0)	86 (1)	411 (13)

Delayed Deaths Caused by Resection. Six additional patients died more than 1 month after right trisegmentectomy (five examples) or right lobectomy (Table 5) for primary malignancy, colon cancer, metastases, and fungal abscess. Although some of these patients were able to return home, hepatic failure was intractable. When these six deaths were included, the overall mortality rate increased from 3.2% to 4.6%, and the operative mortality rate after trisegmentectomy rose from 6.3% to 9.9%.

Postoperative Complications

There were 51 major complications, with some patients having more than one (Table 6). Seven (1.7%) of the 411 patients required re-exploration for postoperative bleeding. Hemorrhage resulted from the cut surface of the liver in six patients and from the cystic artery in one patient. After hemorrhage was controlled, all but two patients recovered without additional complications. The patient

TABLE 4. *Time and Cause of Operative Mortality (Death Within 1 Month)*

Age/Sex	Diagnosis	Procedure	Time of Death	Cause of Death
64/F	Cholangiocarcinoma	RTS	20 days	Hepatic failure Celiac axis thrombosis
22/F	Regenerative nodule misdiagnosed as HCC	RL	4 days	Postoperative bleeding Hepatic failure
50/M	HCC in cirrhosis	RL	0 day	Perforation of CVP Catheter into pericardium, cardiac temporade
63/M	HCC in hemochromatosis	LTS	7 days	Hepatic failure
28/M	Abscess after trauma	RTS	0 days	Hemorrhage
77/M	HCC in cirrhosis	Local	0 days	Myocardial infarction
55/F	Cholangiocarcinoma	LTS	0 days	Hemorrhage
45/M	HCC	RTS	6 days	Hepatic failure Transplant on 6th day
31/M	Trauma	RTS	1 day	Arrythmia due to fat emboli?
52/F	Neuroendocrine tumor (?)	RTS	0 day	Hemorrhage
51/M	Abscess after cholecystectomy	RL	19 days	Sepsis, multiple organ failure
36/F	HCC in cirrhosis	RTS	0 days	Hemorrhage
62/M	Bile duct cancer	RTS	29 days	Liver failure

RTS = right trisegmentectomy.
RL = right lobectomy.
LTS = left trisegmentectomy.

Local = nonanatomical local excision.
HCC = Hepatocellular carcinoma.

who underwent a right lobectomy for pseudohepatoma died of liver failure after re-exploration. A subphrenic abscess developed in another patient who had hemangioma, and was drained successfully. Subphrenic abscesses developed in 24 patients, all after right-sided resection; there was a 15.9% incidence of subphrenic abscess after right trisegmentectomy. The abscesses were drained surgically without delay, usually by a posterior approach through the twelfth rib. Three of the 24 patients died of hepatic failure after adequate surgical drainage.

Prolonged bile leaks was observed in 13 patients, but closed spontaneously without surgical correction within 2 months. Bile leaks occurred in 31.3% of the patients submitted to left trisegmentectomy, a high complication rate that has an anatomic explanation, as previously reported.[10]

After trisegmentectomy, two patients experienced major bleeding from stress ulcers in the stomach and duodenum. They died of hepatic failure a few days after ulcer operations. Other complications, such as deep vein thrombosis, myocardial infarction, cerebral vascular accident, and small bowel obstruction were managed successfully (Table 6).

Follow-up for Benign Lesions

Cavernous Hemangioma. Giant cavernous hemangiomas were excised from 25 males and 75 females ranging in age from 22 to 77 years, with a mean age of 46.2 years. The masses ranged from 4 cm to 41 cm, with a mean of 12 cm in the largest diameter; they were multiple in 21 patients. Focal nodular hyperplasia coexisted in three female patients and hamartoma in two male patients. In eight of the 100 patients, some with and some without symptoms, there was a past history of a malignancy, and the diagnosis before operation was hepatic metastasis.

TABLE 5. *Time and Cause of Early Death Related to Hepatic Resection*

Age/Sex	Diagnosis	Procedure	Time of Death	Cause of Death
64/F	Angiosarcoma Thorotrast cirrhosis	RTS	58 days	Hepatic failure Pulmonary metastasis
59/M	Fungal abscess	RTS	32 days	Sepsis Multiple organ failure
54/M	Hepatocellular carcinoma	RTS	45 days	Hepatic failure
68/M	Hepatocellular carcinoma	RTS	33 days	Hepatic failure
73/M	Hepatocellular carcinoma	RL	32 days	Hepatic failure
71/M	Colon cancer metastasis	RTS	68 days	Hepatic failure

RTS = right trisegmentectomy.
RL = right lobectomy.

Forty-five patients complained of pain in the right upper quadrant, epigastrium, back, or shoulder girdle. Seventeen patients experienced vague but annoying symptoms included dysphagia, abdominal fullness, sensation of pressure, early satiety, nausea, vomiting, fatigue, night sweats, fever, and weight loss. Eleven patients had anemia with a hemoglobin of less than 10 g/dl, three patients had a platelet count of less than 100,000/cu mm, and one patient carried the diagnosis of primary fibrinolysis for several years. Gallbladder disease coexisted in four patients.

The hemangioma ruptured spontaneously in two patients, resulting in hemoperitoneum or hemobilia. Eight patients experienced hemorrhage after unwise percutaneous needle biopsy or open biopsy of vascular lesions. In another 15 patients, hemorrhage occurred spontaneously into the necrotic center of the giant hemangioma,

TABLE 6. *Postoperative Major Complications in Relation to Extent of Hepatic Resection*

	RTS (n = 126)	LTS (n = 16)	RL (n = 110)	LL (n = 48)	LLS (n = 25)	Local (n = 86)	Total (n = 411)
Subphrenic abscess	20	0	3	0	0	1	24
Prolonged bile leak	3	5	3	1	0	1	13
Postoperative bleeding	3	0	1	1	0	2	7
G.I. bleeding	2	0	0	0	0	0	2
Deep vein thrombosis	1	0	1	0	0	0	2
Myocardial infarction	0	0	1	0	0	0	1
Cerebrovascular accident	0	0	1	0	0	0	1
Small bowel obstruction	0	0	1	1	0	0	1
Total	29	5	11	2	0	4	51

RTS = right trisegmentectomy   LL = left lobectomy.
LTS = left trisegmentectomy.   LLS = left lateral segmentectomy.
RL = right lobectomy.   Local = Nonanatomical local excision.
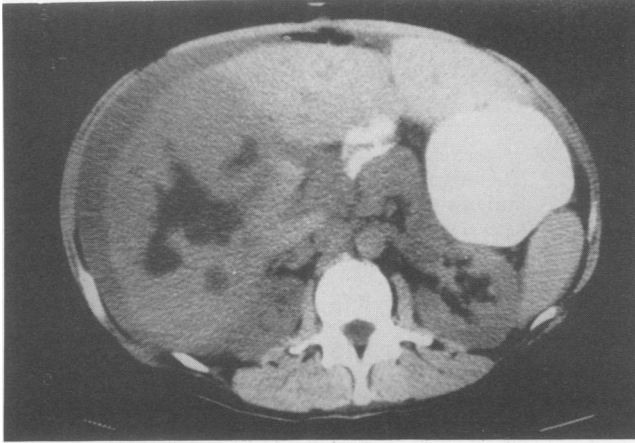
FIG. 3. This giant hemangioma with areas of central necrosis spontaneously ruptured. Emergency right trisegmentectomy was successfully performed.

and in these patients, preoperative dynamic computerized tomography (CT) scan predicted the pathology accurately (Fig. 3). Patients with this complication notice a enlarging palpable abdominal mass or hepatomegaly, accompanied by severe abdominal pain.

In 13 patients, the hemangiomas were almost or completely asymptomatic, but in ten of these patients, the diagnosis could not be made with certainty, despite an extensive work-up. The CT scan of three patients revealed central necrosis and blood clot.
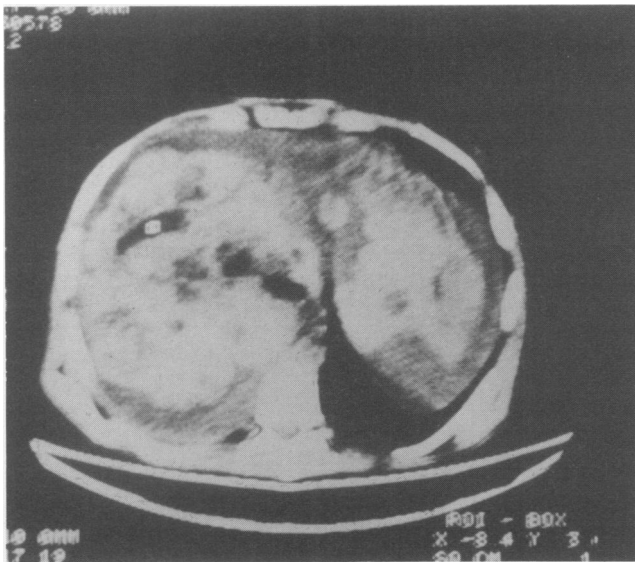

FIG. 4. The multiple liver cell adenoma ruptured spontaneously during close observation. Emergency right trisegmentectomy was performed, leaving several small adenomas in the left lateral segment. Remaining adenomas grew larger, and new adenomas developed. One year after hepatic resection, this patient required orthotopic liver transplantation to relieve severe pain and other mass-related symptoms. She is doing well without recurrence of adenoma 5 years after transplantation.

Thirteen trisegmentectomies, 31 lobectomies, six lateral segmentectomies, and 50 nonanatomic resections were used (Table 3). The trisegmentectomies and lobectomies were reserved for very large lesions (Fig. 3), but some massive hemangiomas could be removed by local excision if they were pendulous or had narrow pedicles.

All 100 patients survived operation and were followed for at least several months, after which further visits were not encouraged. However, 53 patients were traced for this report after 4 months to 14 years (mean of 4.5 years). Four patients died of malignancies that had been diagnosed before hepatic resection: chronic lymphocytic leukemia, testicular cancer, lung cancer and hypernephroma. A fifth patient died from colon cancer that was discovered 6 years after hepatic resection. None of the surviving patients developed late complications other than an incisional hernia in one patient. Two of the patients experienced bouts of acute hepatitis with recovery long after operation.

Before resection, 47 of the 53 patients who interviewed late had experienced significant symptoms. Forty-one were symptom-free, but six patients still had vague abdominal complaints that were different from previous ones. Among the six patients who were asymptomatic before the operation, two had no postoperative symptoms, and the remaining four had died from a previously known malignancy before the follow-up contact. In three patients, small hemangiomas were left unexcised, and none have caused symptoms subsequently.

Hepatic Adenoma. The patients ranged in age from 16 to 60 years, with a mean age of 31.4. Five were male and 17 were female. Ten of the women had a history of using birth control pills or estrogen therapy. Five of the 22 patients, two men and three women, had multiple adenomas. The size of the tumors ranged from 5 cm to 27 cm, with a mean of 11 cm in the largest diameter. One male patient also had a parathyroid adenoma, and one female patient had focal nodular hyperplasia.

Fifteen of the 22 patients had moderate to severe abdominal pain, and four additional patients had vague abdominal complaints. When first seen by us, the adenomas had ruptured in six patients with hemoperitoneum (Fig. 4). Four patients with spontaneous hemorrhage into the necrotic center of the adenoma experienced excruciating pain. Only three patients were asymptomatic, with their solid tumors being found incidentally. These asymptomatic adenomas were excised because of an increase in size, lack of definitive diagnosis, or because it was believed that their presence was reason enough for their removal.

Lobectomy or trisegmentectomy were used for 20 of the 22 resections (Table 3). None of the patients died after operation, and in 20 cases, follow-ups were available on 6 months to 17 years, with a mean of 6.5 years. In three patients with multiple adenomas that involved all four

segments of the liver, some of the lesions were left behind after right trisegmentectomy. In each case, either the remaining adenomas enlarged or new lesions developed. One of these patients died of liver failure 6 years after resection. Five years after resection, another patient died of cryptococcosis, which was part of her acquired immune deficiency syndrome. Another patient who required liver transplantation for massive adenoma regrowth 1 year after right trisegmentectomy is alive and well 5 years after liver replacement (Fig. 4). No other recurrence is known to us at this time. Fifteen patients are free of symptoms after resection, and two others still have vague abdominal complaints that are different from previous symptoms.

Focal Nodular Hyperplasia (FNH). These 17 female patients were 20 to 52 years old, with a mean age of 34.8. Thirteen had used birth control pills. Two patients had multiple lesions. In 17 patients, there was no coexisting benign lesion. The size of the tumors ranged from 4 cm to 14 cm, with a mean of 8 cm in the largest diameter.

Symptoms were milder than those of patients with cavernous hemangioma and with adenoma, and in four patients, the lesions were found incidentally. One patient had had ovarian cancer and another had had a malignant histiocytoma of the skin. In no case was the definitive diagnosis was made before surgery, although the diagnosis was often suspected.

Two trisegmentectomies, four lobectomies, one lateral segmentectomy, and ten local excisions were performed with no deaths occurring. Ten of the 17 patients could be contacted in 1988 after a follow-up of 5 months to 11 years, with a mean of 2.5 years. All of the seven patients who had had significant symptoms were now symptom-free, but three patients still had some vague abdominal complaints. No recurrence of this lesion is known to us.

Congenital Hepatic Cysts. Two patients had widespread polycystic disease, and four others had multiple cysts that were limited to the resected specimen. The remaining ten patients had congenital cysts (Table 2). All of the patients with large cysts had significant symptoms with a history of repeated aspiration of cyst fluid (Fig. 5). Two of the six patients with polycystic disease had required intravenous (I.V.) alimentation and continuous administration of narcotics for nutrition and severe pain. Ten of the 16 patients experienced fever and chills, and four of the patients had jaundice.

Seven trisegmentectomies, five lobectomies, and four local excisions were performed with no mortality. The two patients with severe polycystic liver and kidney disease had right trisegmentectomy or right lobectomy, leaving a lateral hepatic segment or left lobe that had fewer and smaller cysts than the rest of the liver. There was marked symptomatic relief for several years, but eventually there was cystic enlargement of the fragment and its cysts, which returned almost to their original size.
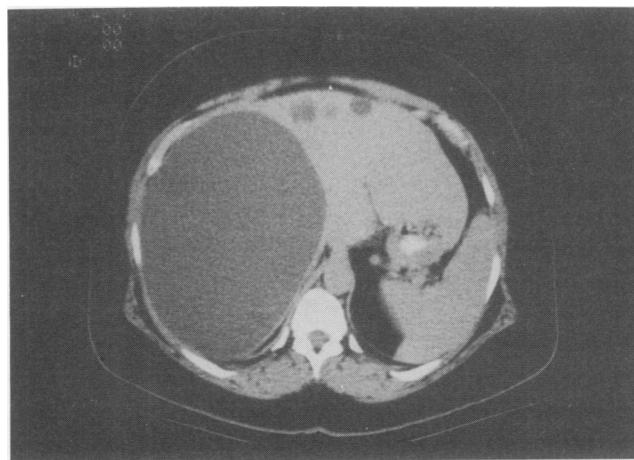

FIG. 5. This large cyst had been aspirated many times and sclerosed several times before excisional therapy.

In contrast to the recurrences that occur with any procedure for widespread polycystic disease, none of the patients whose cyst or cysts could be resected completely has ever had subsequent difficulty with complete follow-ups of 1–15 years.

Four additional patients who were believed to have benign simple cysts proved instead to have malignant changes in the cyst wall. These cases will be considered later in this report.

Other Benign Lesions. The five patients with hydatid cysts underwent trisegmentectomy (one example), lobectomy (3 examples), and one local excision. Two of these patients proved to be unusually difficult cases, since they had been operated upon several times previously. In these two patients, the cysts had ruptured into the biliary tract.

Miscellaneous diagnoses, including trauma, are listed in Table 2, and the procedures used are summarized in Table 3. Of the 27 patients, four died, three of these four deaths being from trauma or prior iatrogenic injury (discussed earlier).

Primary Hepatic Malignancy

The operations performed are summarized in Table 3, and the actuarial survivals of patients with primary hepatic malignancy are shown graphically in Figures 6 and 7. Overall survival rates of 106 patients with primary hepatic malignancy were 84.9% at 3 months, 79.1% at 6 months, 68.5% at 1 year, 53.9% at 2 years, 45.1% at 3 years, 37.2% at 4 years, and 31.9% at 5 years after hepatic resection (Fig. 6).

All of the 12 patients who had had hepatic resection for fibrolamellar hepatocellular carcinoma are alive, nine patients are free of disease 1–15 years after resection, and three patients are living with recurrence 1, 2, and 7 years after resection (Fig. 7). One- to 5-year survival rates of 55
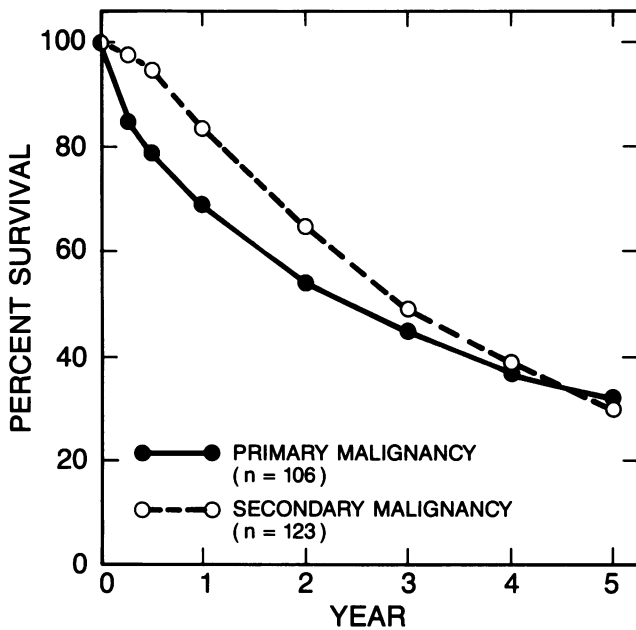
FIG. 6. There was no difference in actuarial survival rates between 106 patients with primary hepatic malignancy and 123 patients with secondary hepatic malignancy after hepatic resection.

patients with nonfibrolamellar hepatocellular carcinoma were 76.2%, 68.2%, 49.0%, 36.7%, and 25.0%, respectively, and those of 14 patients with cholangiocarcinoma were 78.6%, 48.6%, 39.8%, 39.8%, and 39.8%, respectively (Fig. 7).
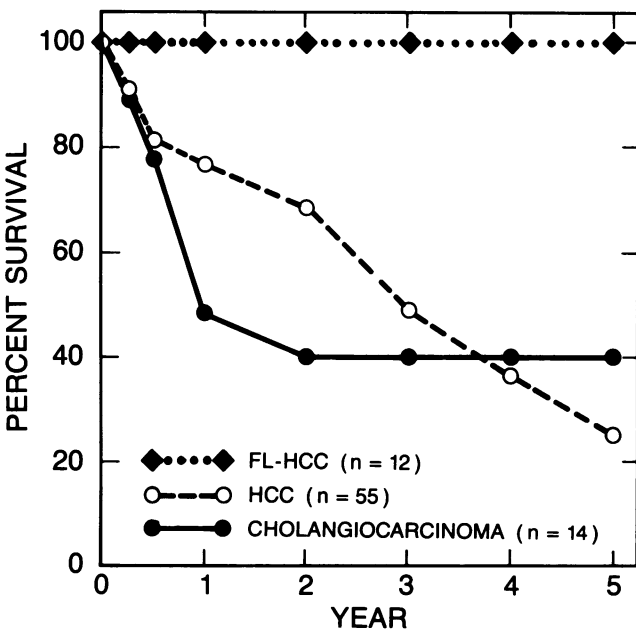

FIG. 7. The survival rate of patients with fibrolamellar hepatocellular carcinoma was higher (p < 0.01) than that of patients with nonfibrolamellar hepatocellular carcinoma and with cholangiocarcinoma after hepatic resection.

TABLE 7. *Fate of 16 Patients with Primary Hepatic Malignancies Who Lived for 5 Years*

Histology	Fibrolamellar†	HCC‡	CHC§	Others‖	Total
Number	5	5	3	3	16
Trisegmentectomy	5	3	2	3	13
Lobectomy	0	2	1	0	3
Died > 5 years	0	2	1	0	3
Time of death (year)	—	8, 8	6	0	—
Living > 5 years	5	3	2	3	13
Survival (years)	6, 7,* 8, 9, 15	7, 7, 12	6,* 8	16, 16, 16	—

* Living with recurrence.
† Fibrolamellar variant of hepatocellular carcinoma.
‡ Nonfibrolamellar hepatocellular carcinoma.
§ Cholangiocarcinoma.
‖ Hepatoblastoma, leiomyosarcoma, rhabdomyosarcoma.

The four patients with single hepatic cysts that had malignant degeneration in the cyst wall were treated by trisegmentectomies in three cases and local nonanatomical resection in one case. The three patients treated with trisegmentectomy died of recurrence of squamous cell cancer 6, 10, and 16 months after trisegmentectomy. The fourth patient, whose solitary cyst contained a small adenocarcinoma, is alive and free of tumor 12 months after local excision.

There were 16 patients who survived more than 5 years after hepatic resection for primary hepatic malignancy (Table 7). The histologic diagnoses were variable. There was an over-representation of trisegmentectomies (13 patients of 16), and in the remaining three patients, lobectomies were performed. Three of the patients died after five years, and two additional patients are living with fibrolamellar disease after 6 and 7 years.

Secondary Hepatic Malignancy

The overall survival rates of 123 patients with hepatic metastasis were 98.3% at 3 months, 95.0% at 6 months, 84.2% at 1 year, 64.7% at 2 years, 48.9% at 3 years, 38.4% at 4 years, and 29.5% at 5 years after hepatic resection (Fig. 6).

The 1- to 5-year survival rates of 90 patients with colorectal carcinoma were 88.1%, 69.3%, 50.0%, 38.9%, and 35.8%, respectively (Fig. 3). Those of 33 patients with metastases other than colorectal carcinoma were 74.4%, 53.7%, 45.9%, 37.6%, and 19.9%, respectively (Fig. 8). The difference in survival rates between the two groups of patients was not significant.

Data from 13 patients who have lived for at least 5 years after resection are summarized in Table 8. Seven are known to be alive after 6–14 years, although one has experienced recurrence. Two more were lost to follow-up, one of whom was free of tumor when, after 8 years, he left our care. Long survival was not associated with larger resections nearly as often as it was in the primary

hepatic malignancies, since only four of these 13 patients had been treated with trisegmentectomy.

Discussion

This large series of partial hepatectomies was collected during a revolutionary period in the history of surgical hepatology, a period during which there were three closely related basic and clinical developments. First, liver transplantation changed from a seemingly unrealizable dream to a highly practical form of therapy.[16,17] Second, research in transplantation stimulated the development of the new field of hepatotrophic physiology, which has greatly increased our understanding of regeneration after partial hepatectomy.[18] Finally, the techniques and expectations of subtotal hepatectomy, as well as the care of patients, after such procedures were refined and extended—often by transplant surgeons who were trying to define the relationship between partial hepatectomy and the new possibility of total liver excision and replacement[19-22]—were remarkably improved.[1,8,10,23,24] The extent to which liver resection has become part of the modern-day armamentarium of oncologists is evident from the plethora of series reported during the last 25 years.[14,15,25-33]

As a corollary, attitudes have changed remarkably about the utility of partial liver removal. Until approximately 15 years ago, the mortality that occurred with any of the major resections was too great to justify their use if a less dangerous, albeit unsatisfactory, alternative was available. This point of view can no longer be supported, and indications for hepatic resections have become far less restrictive for both malignant and benign disease. This was particularly well-illustrated in our series in which 44.3% of the procedures were performed for benign conditions. It was possible to remove giant hemangiomas from 100 patients without a single death's occurrence, and to carry out 22, 17, and 21 resections for adenomas, FNHs, and cystic lesions (including hydatic cysts), respectively, likewise without an occurrence of death. And except for two victims of extensive trauma, one patient with an abscess
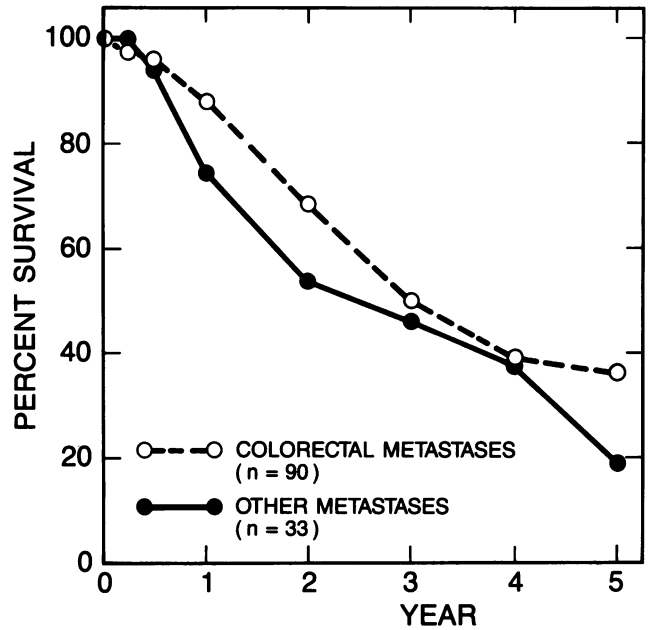

FIG. 8. There was no difference in actuarial survival rates between 90 patients with colorectal metastasis and 33 patients with other metastases after hepatic resection.

caused by prior iatrogenic injury, and one patient with cirrhosis in whom an incorrect diagnosis of hepatoma was made, there was no operative mortality in the treatment of benign lesions.

Because of the remarkable safety of these treatments, it would be easy to have the pendulum swing to the overuse of hepatic resection. One possible stimulus of abuse of resection technology might be the increasing numbers of hepatic mass lesions that are found incidentally by advanced imaging methods. Most of these asymptomatic lesions are histologically benign, and in past years, would have been discovered only at autopsy, if at all. Yet although imaging has allowed patient screening, it has not been effective in defining pathognomonic findings of hepatic lesions other than hemangiomas and cysts.[34-36] Per-

TABLE 8. *Fate of 13 Patients with Hepatic Metastases Who Survived for More than 5-Years after Hepatectomy*

Histology	Colorectal	Carcinoid	Leiomyosarcoma of Stomach	Adrenal Neuroblastoma	Total
Number	9	2	1	1	13
Trisegmentectomy	2	0	1	1	4
Lobectomy	3	1	0	0	4
Lateral Segmentectomy	4	1	0	0	5
Died > 5 years	3	1	0	0	4
Time of death (years)	6, 7, 8†	8	—	—	—
Living > 5 years	4	1	1	1	7
Survival (years)	6,* 7, 8, 14	9	15	15	—
Lost at follow-up (years)	6,* 8	—	—	—	2

* Had recurrence when last seen.   † Died with myocardial infarction tumor-free.

cutaneous needle biopsy often fails to establish a definitive diagnosis because of its limited sampling, and the procedure can cause serious hemorrhage when unwisely performed for vascular lesions.

Our approach to incidental hepatic masses that are less than 3 cm in diameter has been close observation and repeat ultrasonography or CT scan examination if there is no reason to be suspicious of malignancy. Any change in the imaging characteristics of the mass or increases in its size should be a signal for immediate excision. Large incidental tumors, with the possible exception of hemangiomas, usually should be excised.

A case can be made for watching cavernous hemangiomas. Spontaneous hemorrhage from these lesions is not common.[37,38] However, large hemangiomas that are completely asymptomatic are uncommon, provided that a careful history is taken. Hemangiomas exceeding 10 cm in diameter and that have central necrosis can rupture or bleed. Two of the 17 patients in this subgroup in our series had emergency operations for rupture, and eleven others required urgent operations because of an acutely enlarging mass with severe pain (Fig. 4). More and more frequently, we have come to the conclusion that large size alone justifies excision of this type of hemangioma. The possibility of an error in diagnosis is one very important reason not to be too conservative. Three patients in our series who had been believed to have typical imaging characteristics of hemangioma before surgery actually had malignant tumors; there were two hepatocellular carcinomas and one adrenal carcinoma that directly invaded the right lobe of the liver.

Arguments for conservatism in treating adenomas[39] would be harder to sustain. The well-known propensity of these lesions to rupture, causing life-threatening hemorrhage, was seen in almost half of our 22 patients. Our adenoma patient population was heterogenous in that it included five males, and several females who had never received hormone therapy. FNH, which at one time was confused with adenoma,[40] could be watched if the diagnosis were absolutely certain, since these lesions rarely rupture or bleed.[38,41,42] However, the possibility of a missed diagnosis with either adenoma or FNH—even at institutions where experienced and skillful pathologists are available—can be illustrated by our own experience. One of our patients, whose tumor was originally was diagnosed as adenoma, developed bone metastases from his hepatocellular carcinoma two years after right hepatic lobectomy. The diagnosis of FNH was made on frozen section, only to have the final diagnosis of fibrolamellar hepatoma made when the full resected specimen could be studied later. Some of our patients have had an adenoma and FNH in the same liver.

The problem of missed diagnosis was tragically highlighted in four of our patients who had single hepatic cysts,

three of whom had been incorrectly diagnosed and operated on elsewhere. In these three patients, the cysts had been aspirated, and in two of the patients, the cysts had been drained through jejunal Roux limbs. Bloustein and Silverberg have provided detailed pathologic analysis on one such patients.[43] By the time we performed resection, the tumors had spread in three of the four patients, who died after 6–16 months. The only survivor underwent primary local excision and is now tumor-free 12 months later.

Aspiration,[44] internal drainage,[45] marsupialization,[46] fenestration,[47] and sclerotherapy[48] have all been recommended for congenital hepatic cysts. These approaches are no longer justifiable for the treatment of single or localized multiple cysts that can be resected so safely. The same generalization, with some qualifications, might be made about hydatid cystic disease. Although our experience was limited to five cases only, these patients had had multiple previous operations over a period of several years at outstanding clinics, in both the United States and abroad. Increasingly complex problems had developed, such as communication between the dominant cyst and the biliary tract and the growth of satellite cysts. Despite this, however, it was possible at the end of the therapeutic line to excise the cystic disease, although the lobectomies were exceptionally difficult. The presence of many adjacent cysts, as well as fistulas, between the dominant cyst and the biliary tract in the surgical specimen made it obvious that a conservative approach with cystectomy would have been futile.

It is unfair to criticize by today's standards therapeutic decisions that were made for the treatment of cystic disease of any kind many years ago. This is illustrated by two of our own patients with polycystic liver and kidney disease who were submitted to right trisegmentectomy and right lobectomy in 1979 and 1980, respectively. Both had massive hepatomegaly, so extreme in one patient that she was no longer able to eat and could be sustained by I.V. hyperalimentation only. Because the islands of solid hepatic parenchyma were somewhat better represented in the left lateral segment or the left lobe, relief of suffering was achieved with the partial hepatectomies. Both women are still alive, but both have regrown huge cystic livers and may require hepatic transplantation in the near future. If confronted with the same problem today that we faced 9 years ago, hepatic transplantation might be recommended as the first, not the last, step, and consideration would be given to renal transplantation from the same donor. We have already accomplished this in two other patients (Fig. 9).

In management decisions the desirability of examining the relationship between subtotal hepatic resection and total liver removal and replacement will become even more obvious as future strategies to treat patients with

primary and secondary malignancies evolve. In our total collection of resections for both benign and malignant disease, there was a very large percentage of trisegmentectomies. This reflected the advanced state of the pathology. In turn, almost all of the mortality that occurred after trisegmentectomy was caused either by the malignant disease being too extensive to allow safe trisegmentectomy or by there being underlying hepatic disease as an additional adverse prognostic factor. In some of these patients, it was realized too late that the appropriate decision would have been liver replacement instead of a futile and lethal attempt at trisegmentectomy.

The results after orthotopic liver transplantation for malignant hepatic disease have been discouraging.[19-22] Although the survival rate for the first half year has been very high, late tumor recurrence has plagued these efforts. In the past, strong efforts at modern-day adjuvant chemotherapy, treatment with biologic adjuvants, and irradiation have not been systematically tried in liver recipients. Yet liver transplantation can result in the cure of hepatic malignancy on more occasions than the isolated one that has been reported previously.[19-22] As with resection,[12] the most favorable lesions for transplantation are the fibrolamellar hepatomas, and in addition, epithelioid hemangioendothelial sarcomas have had apparent "cures" in about a half of the cases.[20] Even in highly selected cases of metastatic liver disease, significant palliation has been accomplished, and there is now also the prospect of long survival in a tumor-free state.[17,49]

In the past, we have commented that no surgeon should surgically explore a hepatic mass without having the competence to perform all of the major resections, including the trisegmentectomies.[50] The day may have already arrived when liver replacement under strictly defined circumstances should also be part of the obligatory armamentarium.

Lest these remarks be misunderstood, it may be appropriate to conclude by pointing out that, in addition to demonstrating how safely hepatic resection can be performed, our observations have also shown that the real key to reliable treatment of malignant disease will be nonsurgical. Although the yield from an enormous amount of work was substantial in our patients, tumor recurrence was the rule, not the exception. To prevent recurrences, host-tumor relationships will have to be changed. This possibility has been illustrated by experiences—both recent and long ago—with "lymphomatosis" in liver, stomach, small intestine, large bowel, and thoracic organs of transplant recipients. These Epstein-Barr virus-related tumors can necrose completely with discontinuance of immunosuppression and re-emergence of host immune responsiveness.[51-53]

Twenty-five years from now, the most important and practical application of the resectional techniques may be

FIG. 9. Polycystic disease of the liver.

in the treatment of benign disease or for the treatment of mechanical complications from necrosis of malignant lesions caused by biologic or chemical therapy.

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DISCUSSION

DR. WILLIAM P. LONGMIRE, JR. (Los Angeles, California): This review of 411 hepatic resections by Dr. Iwatsuki and Dr. Starzl provides us with a complete analysis of the state of the art of liver resection today. The conditions for which resection may be indicated, some common applications, and the results that can be achieved by the masters of the art give something for the rest of us to strive to achieve.

In their brief historical introduction, Drs. Iwatsuki and Starzl point out that it was only after the precise segmental anatomy of the liver was appreciated that resectional liver surgery began to develop. (Slide) This calls to mind one of the first liver resections that Bill Scott and I reported, almost half a century ago, which was a successfully resected hepatic adenoma that we described as arising in the right and left lobes as it straddled the suspensory ligament of the liver.

It was only after reviewing our article some years later that I discovered that Leon Schlossberg, the medical artist, had provided for posterity evidence of our error; he had seen and had drawn the gallbladder on the right side of the tumor, indicating that our tumor actually lay entirely within the left lobe of the liver.

The authors also commented on the remarkable change in attitude towards liver resection that has occurred during the past two decades, and which is illustrated in the accumulation of their series.

As was pointed out, from 1964 to 1970, only six resections were performed. Four were for benign disease and two for malignant disease, and this has risen exponentially to 78 resections last year alone.

In our first report of liver resection in 1961, there were nine cases, one with death. These numbers had increased by 1983, at the time of the last report from our department by Hillary Thompson, to 138 resections with a 30-day mortality of 10%.

A word of caution should probably be expressed, however, as we enter into this era of "safe hepatic surgery." Care should be exercised to see that resection is not overused for lesions that could be treated by lesser operations. I think many of us would agree that there was a period 15 or 20 years ago when formal hepatic lobectomy was overused in the management of hepatic trauma and that lesser procedures proved more reliable.

Another subject that is brought up in their discussion pertains to the question of when transplantation should be used for some conditions (for example, sclerosing cholangitis, Caroli's disease, polycystic disease, and possibly ductal carcinoma) that are currently treated largely by lesser surgical procedures. The palliative procedures that are now used often make subsequent transplantation much more difficult and, in some cases involving multiple operations, impossible.

As transplantation proves more and more reliable and durable, the selection of the best method of treatment becomes more difficult. I feel