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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,

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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 malignancies, 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%.

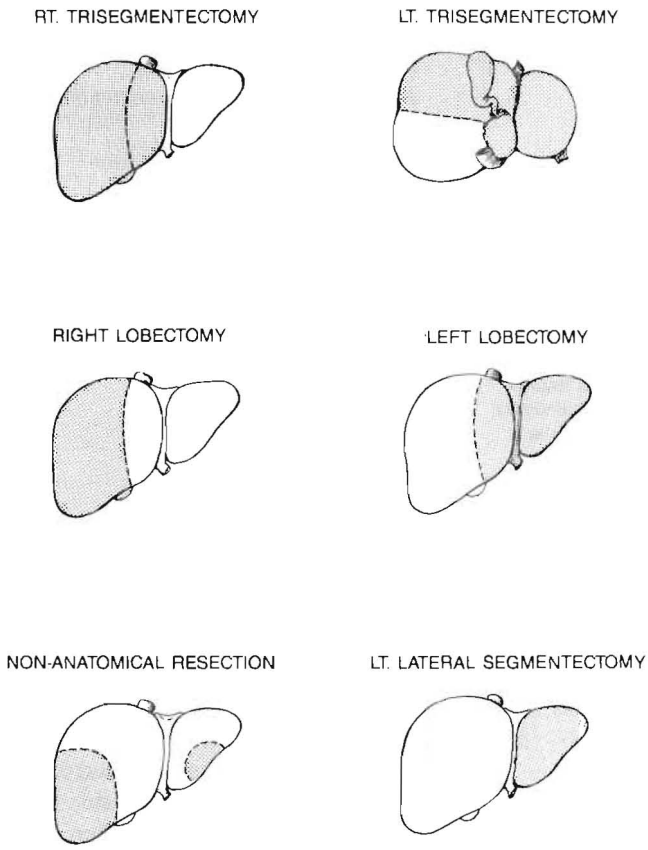

FIG. 1. Six categories of hepatic resections.

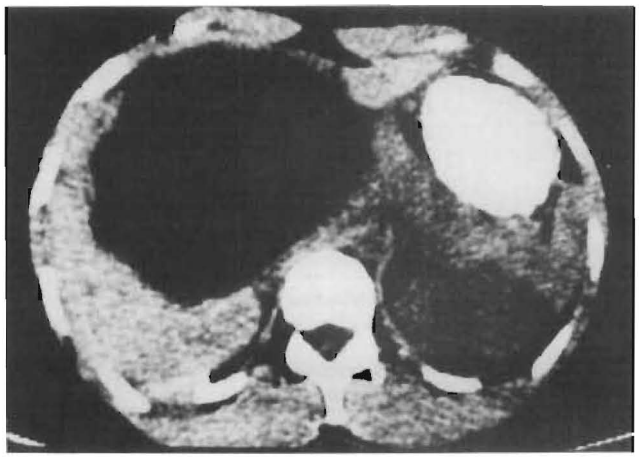

FIG. 2. Nonanatomical local excision of this huge congenital cyst resulted in prolonged bile leak, which ceased 1 month later without surgical intervention.

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
LTS = left trisegmentectomy.
RL = right lobectomy.
LL = left lobectomy.
LLS = left lateral segmentectomy.
Local = Nonanatomical local excision.

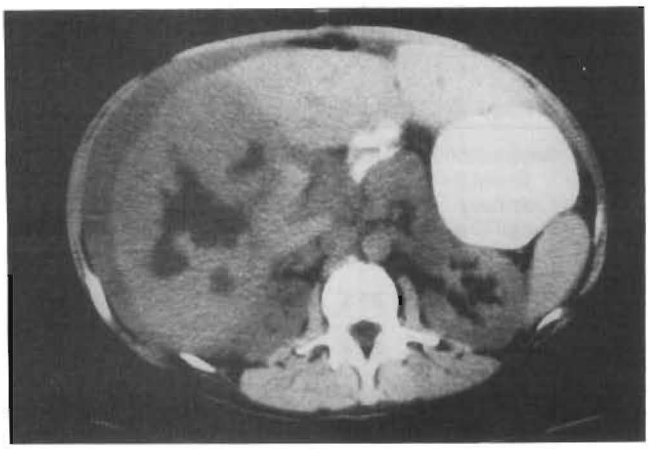

FIG. 3. This giant hemangioma with areas of central necrosis spontaneously ruptured. Emergency right trisegmentectomy was successfully performed.

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.

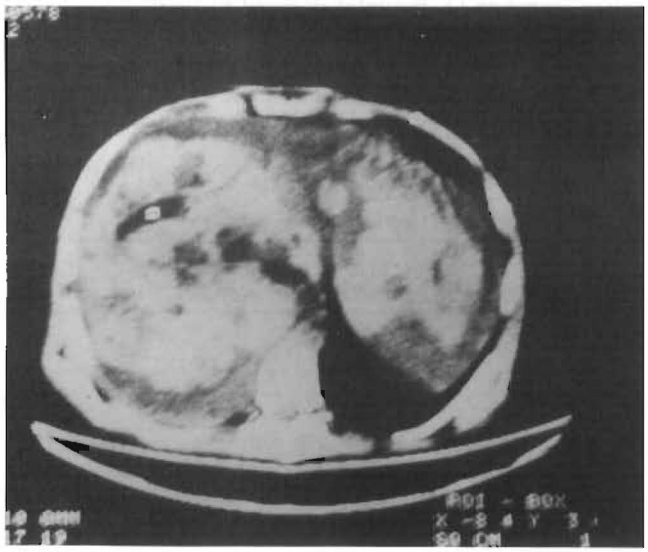

FIG. 4. The multiple liver cell adenoma ruptured spontaneously during close observation. Emergency right trisegmentectomy was performed, leaving several small adenomas in the left lateral segment. Remaining adenomas grew larger, and new adenomas developed. One year after hepatic resection, this patient 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

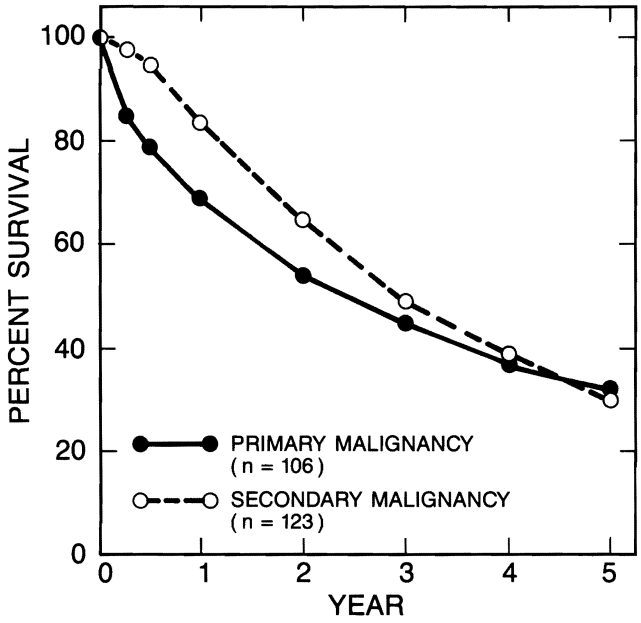

FIG. 6. There was no difference in actuarial survival rates between 106 patients with primary hepatic malignancy and 123 patients with secondary hepatic malignancy after hepatic resection.

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).

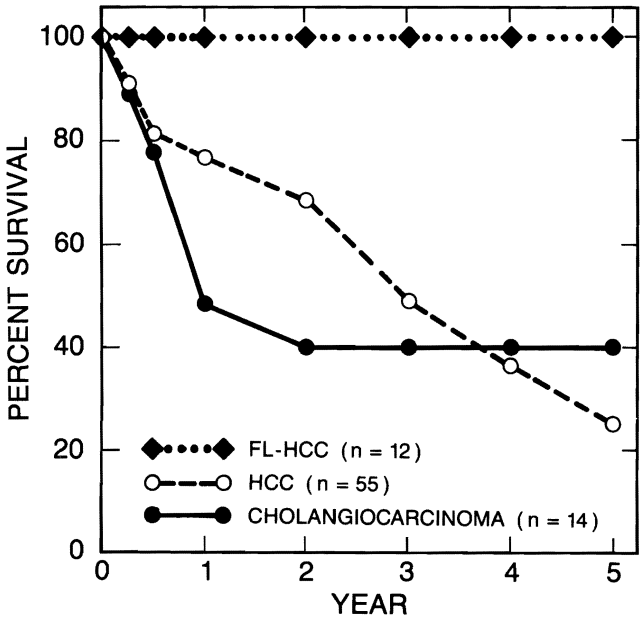

FIG. 7. The survival rate of patients with fibrolamellar hepatocellular carcinoma was higher ($p < 0.01$) than that of patients with nonfibrolamellar hepatocellular carcinoma and with cholangiocarcinoma after hepatic resection.

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 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.

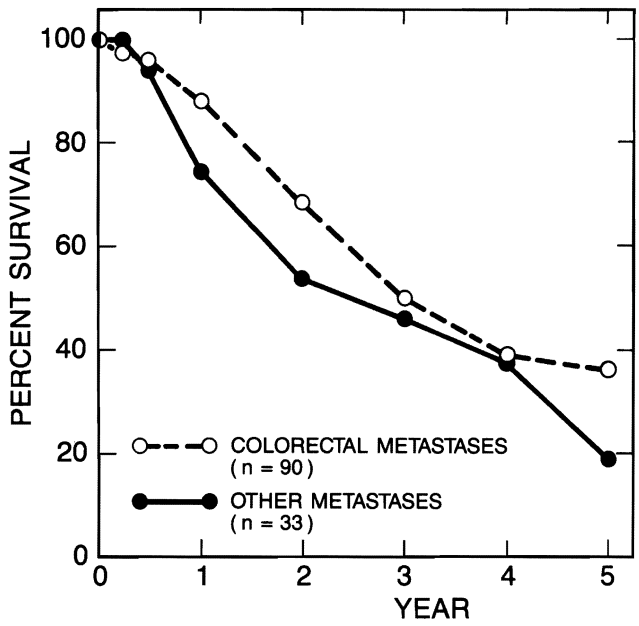

FIG. 8. There was no difference in actuarial survival rates between 90 patients with colorectal metastasis and 33 patients with other metastases after hepatic resection.

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

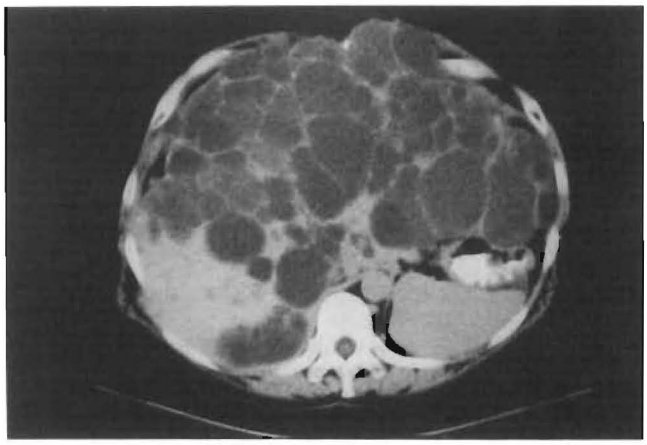

FIG. 9. Polycystic disease of the liver.

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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

quite confident that this review presented today and the recommendations made in the manuscript will help to formulate proper courses of action for the future. I know that in dealing with Dr. Busuttil's very active transplant program, this question arises not infrequently in some of the conditions that I have mentioned.

Our compliments once again to the authors for presenting us with the facts and figures of hepatic surgery of their monumental work of the past 23 years.

DR. MARTIN A. ADSON (Rochester, Minnesota): I am pleased to have been asked to discuss this report, but wish that Doctor Iwatsuki had let me see the manuscript before last night. The use of six categories of resection for management of twelve very different pathologic entities cannot be discussed in 3 minutes—and a thoughtful review of such extensive experience involves more considerations than I was able to think through while sleeping overnight.

Doctor Iwatsuki, I did enjoy your presentation, with its pleasant humor, very much; and just as did the acrobatic lady patient shown on your last slide, you landed on your feet and landed well.

This report demonstrates the feasibility of safe major hepatic resections and reminds us of how much these men have contributed to the anatomic basis of safe resectional surgery of the liver.

I do agree with most of what the authors have said, but I also believe that our views about the role of resectional surgery in the management of some malignancies and some benign tumors may differ philosophically.

My experience involves similar numbers of patients, but differs in two significant ways. First, I have used extended resections (particularly left trisegmentectomy) less often than the authors have. Second, a lesser proportion of resections that I have performed have involved benign disease. Instead, of about one third of the trisegmentectomies, such operations comprise about one sixth of my practice; and instead of 45% of my resections having been performed for benign disease, only about one fourth of the resections I have performed have involved benign disease.

I believe that these differences relate to my concern about the limitations of anatomic solutions to the problems of cancer that are chiefly biological. Also, I have been impressed by the role of the natural history of benign disease.

I am not sure that our attitudes differ so much, and the differences may have something to do with patterns of referral. Still, I think there is a fundamental difference between what *can* be done and what *should* be done. Doctor Bahnson observed in his Presidential Address that what we don't do may be as important as what we do, and Doctor Longmire just referred to the difficulty of decisions that come with technologic change. Years ago, Einstein said that perfection of tools and confusion of goals are characteristics of our time; and the situation has not become much better since he first said this.

Although I cannot ask many of the questions that I have about each specific diesease, there are two questions that I have selected. The first regards the role of left trisegmentectomy in the management of malignant tumors of the liver. The risk of this procedure (even in your hands) is 12%, and half of the patients with malignancies treated with such resections have been observed less than 5 years. Therefore, bearing in mind the great possibility of limited resectional margins, I wonder about the risk-benefit equation. Do you believe that it is truly justified, or are you reserving your opinion until you learn more about long-term survival?

My second question concerns the natural history of benign tumors. I think that 90% of cysts, focal nodular hyperplasia, and cavernous hemangiomas can be safely observed. Decisions regarding whether or not to perform operation are difficult only approximately 5% of the time. The question is: which benign tumors can be safely observed? I am concerned about the half of your resections performed for focal nodular hyperplasia that were very major, and would like to know how such resections can be justified.

I am impressed by your record of safety in the conduct of major hepatic resections. However, I do think that progress also involves knowledge of the true indications for surgery. I hope that the problems of cancer will yield to biological solutions in the future, but even then, we will still need to know more about the natural history of benign disease.

DR. LEON PACHTER (New York, New York): By virtue of a 3% mortality in 400 cases of hepatic resection, the paper presented by Dr. Iwatsuki and Dr. Starzl will no doubt be regarded as a classic in the annals of hepatic surgery.

The majority of hepatic resections in the United States are, for the most part, performed with preliminary hilar and hepatic vein dissection and ligation followed by parenchymal resection.

At New York University, the institutional experience with this technique, as performed by Drs. Localio, Ranson, Eng, and Coppa in 45 patients who had colorectal matastasis to the liver, yielded a 4% mortality, not unlike the experience at Pittsburgh.

(Slide) But in a recent group of 15 additional patients, ten of whom underwent surgery for colorectal metastasis and five for primary lesions, a different technique was used. This is the method that I have used over the past 12 years in 65 patients with severe complex hepatic trauma requiring inflow occlusion. As you can see here, this was accomplished with a mean cross clamp time of 42 minutes, with a range of 28 to 65 minutes. Three of the 15 patients were cross clamped for more than 1 hour. The technique consisted of hepatocyte protection by topical hypothermia and steroids, coupled with prolonged inflow occlusion and resection by the finger-fracture technique of Professor Linn of Taiwan. The mean blood loss here was 100 cc. (Slide) There were no cases of hepatic necrosis. Liver function tests all returned to normal at the time of discharge, and although there was one abscess, there were no deaths.

The maximum time that liver can withstand normothermic or hyperthermic ischemia is presently unknown, but reports from France by Huger and Starzl as well as from others in the United States clearly prove that the 15–20 minutes so frequently cited as the maximum time is clearly a myth.

I would like to ask the authors if they have had any experience with normothermic or hyperthermic ischemia for elective hepatic resections. I would also like to ask them, what was their mean resection time? What was their mean blood loss and what precautions, if any, were used in dealing with the cirrhotic liver?

I enjoyed this paper very much and I feel that the results achieved by the authors have set the standard for all of us to emulate.

DR. WILLIAM V. MCDERMOTT, JR. (Boston, Massachusetts): It was a pleasure to read this impressive series before the presentation, but until I had seen the photographs Dr. Iwatsuki has provided, I had not realized how beautifully he had selected the cases.

I don't believe we can match his series in either volume or quality. Over 15 years, our total series of hepatic resections for malignant disease involved approximately 200 patients, but I will discuss only two subsets that could be compared to the series that Dr. Iwatsuki has just presented. The overall mortality of less than 4% is similar for both series. I would like to comment further on two categories only: 31 primary hepatocellular carcinomas and 76 metachronous cancers from colonic origin. Metastases from other primaries are not included.

Our data and conclusions are very similar to those you have just heard in the excellent report of Drs. Iwatsuki and Starzl. From the group of 76 patients with metachronous metastases, we can present some information that I think emphasizes the relative degree of success of this procedure in treating patients with otherwise incurable disease.

In terms of follow-up, in our group the median survivals were as follows: in Duke's B, those living free of disease, there were 25 total cases, and in Duke's C, there were 21 cases; the actuarial 5-year survival in the Duke's B group was 65%, and that of the Duke's C group was 46%.

We looked at the disease-free interval to see what effect this might have on the prognosis. When the interval was less than 1 year, there was a 56% actuarial death rate with a median survival of 10 months, whereas when the interval was greater than 4 years, the actuarial death rate had dropped down to 25%, leaving us with an overall actuarial survival of 46% for the entire group. The median survival increased steadily with the interval to 24 months when the interval were 2–4 years, and to 44 months when the interval was more than 4 years.

The number of metastases in our series was significant. Eighty per cent of those patients with more than three metastases died of disease before 5 years.

Comparing Dr. Iwatsuki's series with our own, we mentioned their similarity and the mortality. In the primary group, there were 101 primary hepatocellular cancers compared with our 31; their secondary group in-

cluded 118 cases of metachronous cancers compared with 76 in our group.

The actuarial survival rate of our primary group was 57% for 5 years; their series recorded an actuarial survival rate of 88% for 1 year, 62% for 3 years, and 43% for 5 years. In the group with secondary metastases, 65% and 45% of the patients were alive and free of disease at 3 and 5 years, respectively, in comparison with the figures presented by Dr. Iwatsuki of 46% at 3 years and 31% at 5 years. Those are really very excellent results if you think of what the disease would otherwise imply.

Our tentative conclusions are that, in selected cases of primary and secondary cancer of the liver, resection is thoroughly justified and is indicated by the low mortality rates (less than 5%) and the 5-year actuarial survival of 46% in the secondary and 57% in the primary cancers. Also, resection for primary cancer in cirrhotics is indicated only in carefully selected patients because it is in this particular subset that the heaviest mortality will occur and perhaps negate extensive efforts at resection. Finally, the best results (46% at 5 years in metastatic cancers from the colon) will occur in patients having less than 3 metastases, margins greater than 1 cm, an original primary that was a Duke's B classification, and an interval greater than 3 years.

This does not preclude operating on other patients who do not meet these stringent criteria, but I present this criteria only to indicate that this is the gold standard. If one deviates, the overall survival will obviously drop; nevertheless, with thoughtful selection, this is not an absolutely rigid point of departure.

With respect to chromosomal analyses—that is, ploidy—I do not think that it is yet at the stage where this technique can be used in a predictive way.

I certainly enjoyed this extensive series. It was very impressive, and the results were superb, as you have seen.

DR. PAUL H. SUGARBAKER (Atlanta, Georgia): About 3 years ago at the NIH, Kevin Hughes and I collected retrospective data on approximately 850 patients with resected hepatic metastases from large bowel cancer. To be eligible for this study, the patient had to survive a potentially curative hepatic resection from large bowel cancer. We have the Mayo Clinic, Sloan-Kettering, the University of Connecticut, and many other groups to thank for our large body of data (850 patients). We analyzed the data for prognostic factors and patterns of failure, and then intensively studied those patients who survived long-term.

I was surprised by our data regarding prognostic factors, and some of my comments will parallel those of Dr. McDermott. Several factors significantly reduced but did not abrogate survival. Patients with multiple as opposed to solitary metastases did somewhat worse, but not that much worse than the patients with solitary metastases. Positive margin patients did more poorly, yet a good number survived. Some patients with extrahepatic disease, either in the lungs or elsewhere in the abdomen, that was resected at the time of the removal of hepatic tumor survived long-term and were disease-free. A short free interval was a relative but not absolute contraindication to resection. The only clinical feature that we found to be an absolute contraindication to hepatic resection for metastatic disease was the presence of the disease in the lymph nodes draining the hepatic metastases. The phenomenon I call "mets from mets." Therefore I would like to ask our presentor: do you have any absolute contraindications to the resection of metastases from the liver?

My second question comes from my own rather discouraging experience with either right or left trisegmentectomy in the aged patient. I have found that, with the trisegmentectomy procedure, some patients (even though their blood loss was just a few cubic centimeters, as noted in the operative report) sometimes die of liver failure. And so my question is this: do you have an age cut-off when you are performing a trisegmentectomy procedure?

I have a third question: would you go back a second time to remove further hepatic disease? We have anecdotal experience with nine patients who had a second hepatic resection. One of them died after surgery of a myocardial infarction. Eight are doing well long-term after a re-resection of liver metastases months or years after the first hepatic resection. What is your position on this?

DR. JOHN S. NAJARIAN (Minneapolis, Minnesota): I, too, rise to congratulate the authors on an outstanding paper, indeed, probably a seminal paper in the area of hepatic resection. In an active hepatic transplant program, one is fortunate to see patients like these who may benefit from hepatic resection. Trisegmentectomy, as we currently practice it, was actually defined by Iwatsuki and Starzl in the two papers they previously published on this technique.

I have one question concerning a very favorable lesion—namely, the metastatic lesion of colonic carcinoma. Certainly the results are outstanding: from a 30 to 40% 5-year survival, depending on the series you see. Have you had an opportunity to take some of these patients who have had metastases from a colonic carcinoma that is bilobar, and proceed with hepatic transplantation after total hepatectomy?

It would seem that such patients would be the ideal group for this type of therapy. I know you have had some experience in this area. We would like to hear what results you have achieved.

DR. SHUNZABURO IWATSUKI (Closing discussion): First of all I would like to thank all of the discussants for their nice comments and for bringing up some information that I could not deliver today because of the time limitation.

I would like to answer as many of the questions as I can remember. Dr. Najarian asked us if we have done liver transplantation for metastases, particularly from the colon. Yes, we have done liver transplantation for metastases, but not yet for colonic cancer. We are looking for some good candidates with colonic cancer metastases of minimally aggressive biological behavior. We have not yet found an ideal candidate. However, in Europe some cases were treated with liver transplantation, although the results are not good. One of the reasons for poor results is that there is no effective chemotherapy or biological therapy for colon cancer.

The second question is from Dr. Sugarbaker. He asked me the absolute contraindications for resection.

Our general approach is that if we can make a clinically disease-free status by performing a partial hepatectomy and additional resections of lymph nodes, diaphragm, or lung, we do so. I don't believe the term "absolute" is quite right. The prognosis is poor if you treat advanced stages of the disease. However, as we mentioned, there was no operative death from any liver resections for metastases. Therefore, I believe that we are justified in approaching metastatic liver diseases with aggressive surgery. We do not have any age limit for resectional therapy of metastatic tumors. We go back for second resections if the first resection is less than trisetectomy, and the lesion can be excised completely by smaller resections.

Someone asked me about inflow occlusion with the Pringle maneuver. We use the Pringle maneuver for left trisegmentectomy almost routinely. The reason for this is that after trisegmentectomy the cut surface is very large, and hemostasis is rather difficult. We can cross clamp inflow for up to 2–3 hours without any fatal results. However, for small restrictions such as right or left lobectomy, it is not necessary to block the inflow. In other words, blood loss for lobectomy for metastasis is probably one or two units or less.

(Slide) Answering Dr. Adson's questions, this is an hemangioma that we usually see. This is central necrosis, and the patient complained of pain and fever. I believe it is wrong to observe this patient without offering surgery. Of course, we do not remove hemangiomas or cysts in asymptomatic patients if the diagnosis is certain and there is no reason to suspect malignancy.

(Slide) This is a patient with polycystic liver disease. This patient received hyperalimentation because the stomach was compressed and she experienced early satiety. She required continuous narcotic therapy for pain.

(Slide) This is a patient with an hepatoma treated by right trisegmentectomy.

(Slide) This huge region cannot be treated by a left lobectomy alone. You can see a part of the right hepatic vein here. In order to obtain a tumor-free margin, we had to perform a left trisegmentectomy.