# Right Hepatic Lobectomy for Primary Carcinoma of the Liver \*

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In 1899, W. W. Keen <sup>29</sup> in discussing resection of the liver for hepatic tumors said "If we cure 50 per cent of cases of cancer of the breast and 50 per cent of cases of cancer of the rectum, why should we not get as equally good results in cases of cancer of the liver which are well limited with little or no lymphatic involvement?" Many successful cases of local resection and of left hepatic lobectomy for primary and metastatic tumors of the liver have been reported. The surgical removal of the right lobe of the liver has been much slower in development.

The two chief deterrents to surgical excision of the right lobe of the liver have been the technical problem of hemostasis in an organ abundantly supplied with both portal and systemic blood and the lack of knowledge concerning the functional capacity of the remaining hepatic tissue after removal of 60 to 70 per cent of the liver. The excellent study of the anatomy of the liver by Healy et al.24 has established a sound anatomical basis for removal of a lobe or segments of the liver with satisfactory hemostasis and preservation of adequate venous and arterial blood flow and biliary drainage. It has been shown experimentally that 80 per cent of the liver can be removed with little or no detectable alteration in hepatic function.36,37 This fact along with the great regenerative power of the liver 37, 19,28,31 should eliminate the second objection to surgical removal of the right lobe

of the liver. The regeneration does not occur from the cut edge of the liver, but by hyperplasia of the remaining tissue. Both parenchymal and duct cells participate in this process. This has been observed experimentally <sup>19</sup> and in humans.<sup>31</sup>

The first reported attempt at surgical removal of a tumor of the liver was that of Langenbüch <sup>30</sup> in the year 1888. In 1891, Lücke <sup>35</sup> successfully removed a primary carcinoma of the liver. In 1899, Keen <sup>29</sup> reported the first successful resection of a portion of the liver by an American surgeon. The reports on successful removal of the left lobe of the liver and wedge resections of other portions are too numerous to mention specifically. Some of these, however, are listed in the bibliography. <sup>47, 56, 17</sup>

A careful search of the surgical literature to March 1955 revealed 20 reported cases of right hepatic lobectomy. The type of lesion, surgical technic and results are presented in Table I. Only three of the 20 cases reported were primary carcinoma of the liver.

Incidence. Primary carcinoma of the liver is relatively uncommon. Charache <sup>12</sup> reviewed 159,762 deaths which came to autopsy and found an over-all incidence of 0.506 per cent of primary carcinomas of the liver. Primary carcinomas of the liver comprised about 2.5 per cent of the malignant tumors discovered at autopsy in another series.<sup>20</sup> The disease is most common in those countries inhabited by the yellow and dark skinned races,<sup>48</sup> but the incidence appears to be increasing in the Caucasian race.<sup>54, 23</sup> It is most common in middle life

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TABLE I. Reported Cases of Right Hepatic Lobectomy

Surgeon	Date	Technic	Lesion	Follow up
Wendel <sup>62</sup>	1911	Not stated	Metastatic adenocarcinoma	Not stated
Willauer <sup>64</sup>	Oct. 1948	Hilar ligation and cautery	Cancer of gallbladder	Died 3 mo. postop., metastasis
Honjo <sup>25-26</sup>	March 1949	Hilar ligation	Metastatic cancer of rectum	Died 13 mo. postop.
Wangensteen <sup>58</sup>	Nov. 1949	Temporary occlusion afferent blood supply—cautery	Metastatic cancer of stomach	Died June 1950
Wangensteen <sup>59</sup>		Hilar ligation	Metastatic cancer of gallbladder	Died 10 days postop.
Quattlebaum44-45	Jan. 1951	Guillotine transection	Angioma of liver	Alive and well, 4 yrs., 3 mo
Brunschwig <sup>10</sup>	June 1951	Not stated	Angioma of liver	Not stated
Brunschwig <sup>10</sup>	Jan. 1951	Not stated	Angioma of liver	Not stated
Quattlebaum44-45	Feb. 1952	Guillotine transection	Angioma of liver	Alive and well, 3 yrs.
Quattlebaum44-45	Feb. 1952	Hilar ligation	Hepatoma	Died 19 mo. postop., metastasis
Lortat-Jacob34	April 1952	Hilar ligation	Metastatic cancer	Not stated
Brunschwig <sup>10</sup>	May 1952	Not stated	Hepatoma	Not stated
Pack <sup>42</sup>	Dec. 1952	Hilar ligation	Plasma cell granuloma	Alive and well Nov. 1954
Bowden <sup>8-9</sup>	May 1953	Hilar ligation	Metastatic leiomyosarcoma	Alive and well May 1955
Pack <sup>43</sup>	Oct. 1953	Hilar ligation	Cancer of gallbladder	Died March 1954, metastasis
Lorimer <sup>32–33</sup>	Dec. 1953	Hilar ligation	Mesenchymoma	Recurrence April 1955— has known metastasis
Mersheimer <sup>39-40</sup>	Jan. 1954	Hilar ligation	Hepatic embryoma	Alive and well April 1955
Mersheimer <sup>39-40</sup>	Feb. 1954	Hilar ligation	Hepatoma	Died Jan. 1955, recurrence
Pack <sup>43</sup>	Feb. 1954	Hilar ligation	Cancer of gallbladder	Died 7th postop. day
Pack <sup>43</sup>	Aug. 1954	Hilar ligation	Cancer of gallbladder	Alive and well Nov. 1954

but occurs in all age groups.<sup>48</sup> Wilbur <sup>63</sup> reported a neonatal case with metastasis to the humerus. The incidence is higher in males. The right lobe of the liver is most frequently involved.<sup>55</sup>

Etiology. Many authors report a higher incidence in patients with cirrhosis than in the general population.4, 18 In a report of 1,073 cases of primary hepatic carcinoma. Berk and Lieber 6 found cirrhosis in 61 per cent of the cases. In this same study, 1,989 cases of hepatic cirrhosis were reviewed. Primary hepatic carcinoma occurred in 4.5 per cent. Hepatic cell carcinoma more often accompanies cirrhosis than does carcinoma of the bile duct.27, 22 Hoyne cites Wu and Kang 65 who postulate that carcinomas of the liver may be more frequent than carcinomas of the bile duct because of a more active regeneration of the hepatic cells than of those of the bile duct. Nodular hypertrophy of the liver, however, is not a uniform occurrence in those cases of cirrhosis

which develop carcinoma. Other predisposing factors which have been considered are diet, alcohol, chronic irritation, parasites, syphilis, congenital or hereditary factors, chemicals, hemochromatosis, trauma, venous congestion and inflammation.<sup>4</sup> A few cases of primary carcinoma of the liver have been reported following viral hepatitis.<sup>57</sup>

Pathology. Three types of primary hepatic carcinoma occur: (1) Hepatoma arising from the polygonal cells of the liver; (2) Cholangioma arising from the epithelium of the small bile ducts; (3) A mixed type containing microscopic features of both, a very small group. The frequency of metastasis is difficult to evaluate adequately and reports vary markedly in this regard. Some report extrahepatic metastases occurring relatively infrequently, 2, 21 while in other series extrahepatic metastases have occurred in 75 per cent of the cases. Most reported series are based on autopsy findings and the rate of antemortem diagnosis is

low, so that most cases follow the natural course of malignancy unless death supervenes from loss of vital function of the liver before metastasis can occur. Early invasion of the intrahepatic blood vessels is more common with hepatoma while extrahepatic metastases are more frequent with cholangioma.12 Metastases are noted more frequently in the lungs than in the regional lymph nodes.48,54,49 Less common sites of metastasis are the diaphragm, pleura, bones, omentum, peritoneum, intestinal wall, skin, brain, spleen, adrenal glands, pancreas, hepatic veins, portal vein and right auricle. Anglesio 3 reported a case of primary carcinoma of the liver with metastasis only to the ribs and vertebra. In a review of 1.391 cases, metastases in long bones occurred in 33 per cent.11

Diagnosis. There is no clear-cut symptom complex which would enable one to make the diagnosis of primary hepatic carcinoma. Abdominal pain of varied location and, at times of vague character, has been reported as the most common initial symptom. 48, 49, 13 Wilbur, 63 in a review of 40 cases, reported abdominal pain clearly present in 72.5 per cent and definitely absent in only three cases. The pain is frequently in the epigastrium or under the costal margins and may be referred to the back or chest. Its character is as varied as its location. sharp or dull, constant or intermittent, mild or severe. The symptoms of indigestion are not characteristic and vary from nausea and vomiting to postprandial distress or distention. Weight loss is a prominent symptom often accompanied by weakness.13 Fever and chills occur in a significant number of cases. Melena and hematemesis from ruptured esophageal varices have occurred as has hemoperitoneum due to hemorrhage from the tumor into the peritoneal cavity. Nadler and Wolfer 41 were the first to report a case in which spontaneous hypoglycemia was caused by a primary carcinoma of the liver and this has subsequently been reported by others.16, 5, 38

Physical Examination. The single most striking physical finding is a palpable abdominal mass. The enlarged liver is frequently tender and may be smooth or nodular. Jaundice occurs in many cases and is usually mild. Ascites of varying degree has been reported to occur in almost half of the cases. Hemorrhoids, and other evidence of collateral circulation, may be present. Edema of the lower extremities may occur before or after the development of ascites. Rosenberg 48 reported a few cases with a bloody pleural effusion on the right side with no evidence of metastasis to the pleura or to the lung parenchyma. In the case we are reporting, there was a right pleural effusion without evidence of pulmonary metastasis at the time of operation.

Laboratory Studies. Many authors make the statement that routine laboratory studies are of little aid in the diagnosis of primary hepatic malignancy. Because of the large functional reserve of the liver and the limitations of the available methods of study, it is possible for large amounts of hepatic tissue to be involved with no laboratory evidence thereof. Studies indicating decreased hepatic function are not diagnostic of the extent of involvement by hepatic malignancy, especially since so many hepatic carcinomas occur in previously damaged livers.

Roentgenography. There are no pathognomonic roentgenographic findings. roentgenogram of the abdomen may reveal hepatomegaly. Intrahepatic calcification is suggestive, but not specific in view of the many other causes. A case of hepatoma with diffuse calcification of the right upper quadrant has been reported.14 Displacement of the stomach, small intestine, colon, or kidney may be demonstrated by appropriate films.51 The right diaphragm may be elevated and its movements restricted. 61, 51 Roentgen examination with the aid of artificial pneumoperitoneum has been recommended as a means of demonstrating masses in the region of the liver, but has been of limited and questionable value.<sup>51</sup> The use of thorium dioxide as an aid in diagnosis has been suggested.<sup>7</sup> However, it is of limited value and entails the danger of late hepatic damage. Other radioactive substances, such as radioactive iodinated human albumin, have had limited clinical application, but hold future promise as an aid in diagnosis.<sup>53</sup> Translumbar aortography or splenoportography may also be helpful. Biligrafin studies have not been performed in enough cases to determine its value, but it may prove to be a valuable diagnostic aid.

Biopsy. Ward 60 reports the use of needle biopsy in 111 cases of proven primary and secondary hepatic carcinomas. The lesion was demonstrated in 74 per cent of the cases. A positive needle biopsy is an unequivocal finding, but a negative biopsy does not rule out the possibility of malignancy and repeated biopsies are indicated if the lesion is suspected. Two disadvantages of needle biopsy are the possibility of being misled by a histologic report which is positive for cirrhosis and negative for tumor, and the more serious possibility of tumor implantation along the site of the needle biopsy as has been reported in other tumors.1 Peritoneoscopy with liver biopsy is another possible adjunct to the diagnosis and may be useful in doubtful and poor risk cases.

Exploratory laparotomy will give the highest per cent of correct early diagnosis as well as evidence of resectability. Any patient in whom primary hepatic carcinoma is suspected, who is able to tolerate the procedure, should have early laparotomy if earlier diagnosis and a significant survival rate is to be achieved.

### CASE REPORT

A 47-year-old white woman was admitted to the medical service of the Jefferson Medical College Hospital on December 3, 1954. Seventeen months before admission she developed vague epigastric pain. Three months later, melena occurred and a duodenal ulcer was demonstrated. Medical



Fig. 1. Intravenous urogram revealing large smooth mass in right upper quadrant depressing the right kidney.

therapy was effective and she became asymptomatic.

Two months before admission she felt a tender mass in the right upper quadrant of her abdomen and had pain radiating through to the back, accompanied by fever, nausea and vomiting. Her symptoms subsided with antibiotics. Ten days later she had chills, weakness, anorexia, right pleuritic pain, fever and moderate anemia. A right pleural effusion was noted on x-ray. She did not improve with antibiotics and blood transfusions and after the development of right shoulder top pain she was transferred to the Jefferson Hospital. At this time, she had lost 30 pounds. There had been no fatty food intolerance, flatulent indigestion, jaundice, pruritis, or change in the color of stool or urine. She had never used alcohol.

The presence of rheumatic heart disease had been established at the age of 12. When she was 25, a cesarean section had been performed near term because of congestive failure. She continued to take digitalis regularly for five years and intermittently since that time.

The patient was a thin, white, chronically ill woman in no acute distress. There was flatness, and breath sounds were not heard, at the right base. The heart was enlarged to the left anterior axillary line and a faint, soft systolic murmur and an accentuated first sound were heard at the mitral area. The second pulmonic sound was accentuated. The liver was palpable 4 finger-breadths below the costal

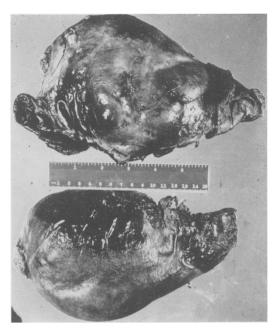


Fig. 2. For description see text.

margin with a firm, rounded, 4 cm. nodule on its free edge. The spleen was not felt. Rectal and pelvic examination were negative.

The patient had a low-grade, intermittent fever throughout her hospital stay. Pertinent laboratory studies were as follows: Hemoglobin 11 Gm. RBC 3.7 million, WBC 13,000 with normal differential, urinalysis normal, BUN 7.4, FBS 72. Electrocardiogram demonstrated a first degree heart block.

A right pleural effusion was evident on x-ray examination. A thoracocentesis yielded 300 ml. of dark amber, sterile fluid with 5.3 Gm.% protein and no neoplastic cells. The right kidney was displaced downward by a large smoothly outlined mass in the right upper quadrant (Fig. 1).

She was transferred to the surgical service, and an exploratory laparotomy was performed Dec. 24, 1954, through a right subcostal incision. A large, smooth mass, grayish white in color, occupied most of the enlarged right lobe of the liver. The mass presented from the inferior surface, the anterior surface being relatively smooth. Two separate, discrete, hard nodules, the larger measuring 4 cm., projected from the inferior border. The 2 nodules were excised. The diagnosis on frozen section was malignant hepatoma. There was no evidence of intraperitoneal metastasis. The right pleural cavity was then opened and the lung and diaphragm carefully inspected. No intrathoracic metastasis was found.



Fig. 3. For description see text.

The right lobe of the liver was then removed using a technic to be discussed later. Upon transection of the hepatic veins, cardiac arrest occurred. Cardiac massage through the right pleural cavity for approximately 2 minutes restored cardiac action. No attempt was made to cover the raw surface of the liver. An intercostal drainage tube and 2 large Penrose drains were placed and the pleural and abdominal wounds closed in layers. The patient received 3,500 ml. of whole blood during the procedure.

The surgical specimen consisted of approximately two-thirds of the liver composed of the right lobe. Together with the gallbladder it weighed 1,600 Gm. (Fig. 2). The capsular surface was pink-red to tan and multinodular. Hemi-section of the mass revealed a large, circumscribed, light yellow to tan, eccentric peripheral area which measured  $11\times 10$  cms. (Fig. 3). Fibrous encapsulation and trabeculation with central necrosis were apparent. Three to 4 cms. of normal hepatic tissue extended beyond this tumor to the severed border of the specimen.

Histologically, 3 distinct features contributed to the diagnosis of malignant hepatoma, predominantly hepatic cell type. Some 70 per cent of the malignant cells mimicked polygonal hepatic parenchyma. About 20 per cent simulated biliary ductal structures. A transitional region, a mixture of these two elements, completed the picture. A



Fig. 4. For description see text.

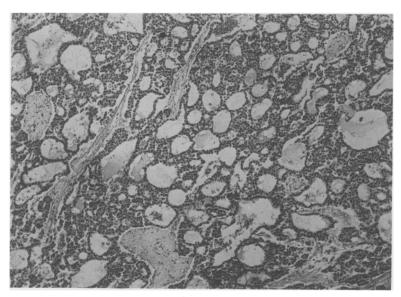


Fig. 5. For description see text.

rather homogeneous collection of typical hepatic cells were seen on microscopic examination (Fig. 4). Some were arranged in irregular cords while others formed a mosaic pattern. Noticeably deficient were portal areas and lobular septal divisions. Individual cells varied from normal to several times this size. Many of the cell borders were indistinct. The cytoplasm was moderately abundant, homogeneous and granular. Nuclei were predominantly single and many possessed perinuclear haloes. A minimum of supportive stroma was present.

In other regions, especially adjacent to its dense, fibrous capsule, the cellular configuration was strikingly different. There were proliferative, irregular, cubiodal cells displaying a tendency to reproduce biliary ducts (Fig. 5). The cytoplasm was scant and vacuolated, whereas the nuclei were large, round and hyperchromatic. Supportive stroma was moderately prevalent in this cholangiolar portion of the tumor. Of unknown significance, but perhaps of prognostic import, was the dense, fibrous capsule buttressing the outermost cells and inter-



Fig. 6. For description see text.

posed between neoplasm and normal hepatic parenchyma (Fig. 6).

Mixed cell types of the above-described elements were interspersed between representative areas described. These formed a gradual transition between the hepatocarcinomatous and cholangio-carcinomatous portions of this malignant hepatoma.

The postoperative course was benign and the intercostal tube was removed on the second day and the drains were shortened on the fifth day and removed on the tenth. There was no drainage of bile at any time. The wound healed nicely (Fig. 7).

The patient was discharged on the twenty-second postoperative day. She has been followed for 12 months and is enjoying good health with no sign of residual tumor. Her laboratory studies continue to be within normal limits.

Surgical Anatomy. The surgical anatomy of the liver, as pointed out by Healey,<sup>24</sup> is similar to that of the lung. There is a segmental distribution of the bile ducts, hepatic arteries and portal veins and the large hepatic veins have an intersegmental course (Figs. 8 and 9). Careful injection studies of these systems reveal a segmental topography separated into a right and left lobe. The left lobe consists of a medial and lateral segment and the right lobe an anterior and posterior segment.

In removing the right lobe of the liver, extrahepatic ligation of the portal and systemic vascular systems as well as the biliary system can be performed and the lobe removed across a relatively avascular interlobar plane. The hepatic veins in the intersegmental plane serve as landmarks in the parenchymal dissection. The hepatic venous drainage into the inferior vena cava is variable.24 The right hepatic vein drains directly into the right side of the vena cava. The middle and left hepatic veins usually join in a common trunk entering the left side of the vena cava. There are other small branches which may be encountered. Extrahepatic ligation of the hepatic veins has been reported by Pack. 42 This is dependent upon how much of the vein can be exposed in the fosa of the vena cava.

Surgical Technic. In reviewing previous cases of right hepatic lobectomy, various incisions and combinations of incisions have been described. Adequate exposure is of primary importance. The right thoracoabdominal incision described by Satinsky 50 affords satisfactory exposure of the porta hepatis, entire right lobe of the liver and the supra- and infradiaphragmatic areas.

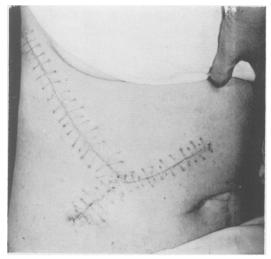


Fig. 7. For description see text.

In our case, a combination of a right subcostal and an eighth interspace incision resulting in an inverted "T" was utilized. The lower portion of the incision may be performed first for abdominal exploration and the diagnosis and the local resectability of the lesion established. The eighth thoracic interspace can then be opened. The diaphragm is incised posteriorly in line with the incision to the inferior vena cava at the superior margin of the liver.

The peritoneal reflections and ligaments of the liver are divided and the entire right lobe rotated and delivered into the thorax. The cystic duct and artery are doubly liated and divided. The right hepatic duct, right hepatic artery and right branch of the portal vein are ligated close to the liver substance and divided.

The parenchymal dissection commences just to the right of the falciform ligament through the interlobar fissure which runs along an imaginary line from the gallbladder fossa below to the fossa of the inferior vena cava above. The capsule of the liver is cut by sharp dissection, but after the capsule is divided blunt dissection by means of the finger or back of the scalpel may be utilized. Oozing from the cut surface of the liver is brisk and can be controlled by pres-

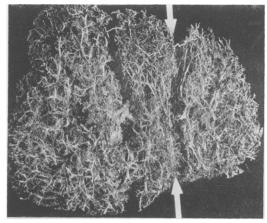


Fig. 8. Injection mold of hepatic arterial, portal venous and biliary ductal systems prepared by Healey. Arrows indicate fissure formerly believed to separate right and left lobes. The true fissure lies to the right.

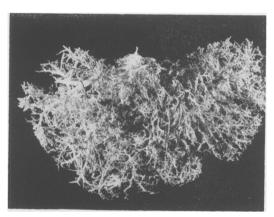
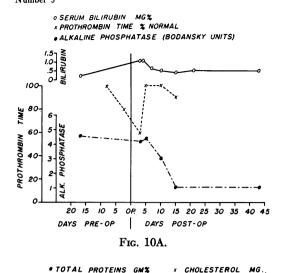


Fig. 9. Injection mold prepared by Healey as in Fig. 8 with injection of hepatic venous system in addition, resulting in obliteration of the anatomical fissures.

sure until individual ligation of the bleeding hepatic veins is accomplished. In our case, mass ligatures of the liver added very little to hemostasis. After dissection of most of the parenchyma, the inferior vena cava is visualized and the hepatic veins are identified. Extrahepatic ligation of the tributaries of the right hepatic vein is next performed if enough of the vein is exposed. If, as is our case, the veins are intrahepatic, the rest of the parenchyma is sectioned and the veins individually ligated after division. The raw surface of the liver is not covered. The right pleural cavity is drained by the



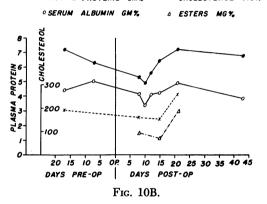


Fig. 10. Graphs of liver function studies. Note decrease in the level of total proteins occurring at the expense of the albumin fraction on tenth post-operative day.

use of a soft latex tube and a water seal, and two large filled Penrose drains are placed near the cut edge of the liver and brought out the lower angle of the abdominal wound.

Preoperative Preparation of the Patient. The main goal of management is to improve hepatic function as much as possible and to protect the functional hepatic tissue during and after operation. A high caloric, high protein, high carbohydrate diet should be given. In order to insure maximum glycogen deposition in the liver preoperatively, ten per cent invert sugar, or dextrose and insulin may be given intravenously for several days prior to operation. Vitamin K

should be administered if the prothrombin time is low. Because of the susceptibility of the liver to anoxia, 46 existing respiratory disease, cardiac decompensation or anemia should be treated. 61 Preoperative sedation should be minimal and the same precautions observed regarding narcotics as will be discussed under postoperative care.

Postoperative Care. The use of invert sugar in intravenous fluids is of value. It has been shown experimentally that fructose is more rapidly and effectively converted into liver glycogen than are dextrose and other sugars.15 It is said to be superior to dextrose in its nitrogen sparing effect.2 Since a greater caloric intake is achieved with ten per cent invert sugar solution than five per cent fructose, the former solution should be utilized in the postoperative period. Crude liver extract should be administered parenterally. An adequate diet contains all necessary vitamins and lipotropic substances, so that the use of crude liver extract may be terminated when a satisfactory oral intake is established. Adequate oxygenation during and after operation must be maintained,46 and episodes of hypotension avoided. A wide spectrum antibiotic should be given.

When the patient is able to resume oral feeding, a high caloric, high protein, high carbohydrate diet should be given to protect against further hepatic damage and furnish material for regeneration of liver substance, Vars and Ravdin 46 added fat to an already adequate diet while maintaining the protein fat ratio. They noted increased liver protein regeneration and a more positive nitrogen balance. Brewer's yeast tablets provide a satisfactory source of vitamin B complex. The use of salt free albumin should be restricted to those cases who have a diminution of serum albumin to the critical level. In our patient, hypoproteinemia was noted about the tenth postoperative day (Fig. 10) as reported by Pack.42 The greatest reduction occurred in the albumin fraction.

Barbiturates and narcotics should be used only when needed and with extreme caution. Small doses of the long-acting barbiturates which are excreted by the kidney are safer to administer than the short acting barbiturates detoxified by the liver.<sup>52</sup>

## DISCUSSION

Primary carcinoma of the liver can be successfully treated surgically. With the accumulation of knowledge of the surgical anatomy, physiology and regenerative capacity of the liver, a more aggressive attitude toward primary hepatic tumors is justified. We, as well as others, have demonstrated that total hepatolobectomy can successfully be accomplished in humans. That this is only the fourth reported right hepatic lobectomy for primary hepatoma is perhaps in part due to the difficulty of diagnosis by means short of exploratory laparotomy. The segmental structure of the liver as demonstrated by Healey et al.24 lends itself to anatomical dissection with minimal danger of postoperative bile drainage or uncontrollable hemorrhage. Drainage of bile did not occur in our patient.

When the ultimate prognosis in the untreated case is considered, the desirability of early surgical intervention in all but extremely poor risk patients suspected of having primary hepatoma is evident.

# SUMMARY

- 1. A case of successful right hepatic lobectomy for primary hepatoma is presented and the literature reviewed.
- 2. The importance of early exploratory laparotomy in diagnosis and treatment is emphasized.

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#### ADDENDUM

The patient was followed regularly in the outpatient department. In March of 1956, 15 months following operation, a mass was again palpable in the epigastrium. Laparotomy at that time revealed metastatic carcinoma of a similar histologic pattern in the hypertrophied left lobe of the liver.

The patient was last seen in June of 1956. She had gained 30 pounds since the original operation and was carrying out her usual activities.

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