Hepatic Morphology in Cardiac Dysfunction

A Clinicopathologic Study of 1000 Subjects at Autopsy

JOSEPH M. ARCIDI, Jr., BS,
G. WILLIAM MOORE, MD, PhD, and
GROVER M. HUTCHINS, MD

From the Department of Pathology, The Johns Hopkins Medical Institutions, Baltimore, Maryland

Chronic passive congestion (CPC) and centrilobular necrosis (CLN) are well recognized pathologic changes, but their exact relationship to different forms of cardiac dysfunction is uncertain. We reviewed clinical data and hepatic, renal, and adrenal morphology related to cardiac dysfunction in 1000 autopsy subjects at The Johns Hopkins Hospital whose hearts had been studied after postmortem arteriography and fixation in distention. Fourteen pathologic variables, including body and organ size, and microscopic changes graded on a semiquantitative scale, and 18 clinical variables including congestive heart failure, shock, and cardiovascular disease, were analyzed statistically. Distinct patterns of cardiac dysfunction emerged for the two spectra of hepatic morphologic change. Among patients with variable CPC, but slight or absent CLN, the amount of CPC was predicted in a multivariate analysis by severity of right-sided congestive heart failure. CPC severity correlated with cardiac weight and chamber enlargement ($P < 0.001$). Among patients with variable CLN, but slight or absent CPC, CLN was predicted by profound hypotension and by renal failure. In addition, CLN, but not CPC, was significantly correlated with renal acute tubular necrosis ($P < 0.001$) and adrenal cortical medullary junction necrosis ($P < 0.05$), two lesions associated with shock. Among all 1000 patients CPC and CLN were highly significantly correlated ($P < 0.001$). The results show that hepatic CPC arises from conditions producing elevated systemic venous pressure but that CLN arises from reduced systemic arterial pressure; and the presence of one potentiates the development of the other. (Am J Pathol 1981, 104:159–166)

HEPATIC CHRONIC PASSIVE congestion (CPC) and centrilobular necrosis (CLN) are commonly encountered at autopsy and generally imply an abnormality of cardiac function. Chronic passive congestion is usually regarded as a consequence of right-sided heart failure, while centrilobular necrosis is considered a consequence of severe hypotension or shock. These two morphologic observations are often seen together, and some authors have emphasized the importance of synergistic processes.[1,2] In the present study, we sought to clarify these relationships by correlating the clinical features of cardiac dysfunction with their morphologic manifestations at autopsy.

Materials and Methods

We reviewed the findings in 1000 consecutive adult (>15 years old) patients on whom autopsies were performed at the Johns Hopkins Hospital, whose hearts had been studied after postmortem coronary arteriography and fixation in distention.[3] The autopsies took place between 1967 and 1977, and, in general, in the cases represented there had been clinical expectation of cardiac disease. This group comprised 19% of adult autopsies performed during this period. Eighteen clinical variables, including the duration and severity of right- and left-sided congestive heart failure, the duration and severity of shock, and features associated with cardiovascular disease, such

Supported by NIH Grant LM-03651 from the National Library of Medicine with HL-17655 from the National Heart, Lung and Blood Institute.

Presented in part at the 69th Annual Meeting of The International Academy of Pathology, New Orleans, Louisiana, February 26, 1980.

Dr. Moore is a Research Fellow of the American Heart Association, Maryland Affiliate, Inc.

Accepted for publication April 17, 1981.

Address reprint requests to Dr. Grover M. Hutchins, Department of Pathology, The Johns Hopkins Hospital, Baltimore, MD 21205.

0002-9440/81/0807-0159$00.90

as hypertension, diabetes mellitus, and chest pain, were abstracted from the patient's medical records. No attempt was made to reinterpret the diagnoses of the attending clinicians.

The clinical severity of left-sided congestive heart failure, right-sided congestive heart failure, and hypotension were each graded on a semiquantitative scale ranging from 0 (no disease) to 4+ (maximum severity). The degree of left ventricular failure was established on the basis of physical symptoms and clinically documented pulmonary vascular disease. The severity rating was a composite of these factors. For left-sided congestive failure, a severity of 1+ was assigned in the case of mild or episodic shortness of breath and dyspnea on exertion; a severity of 2+ was assigned for moderate shortness of breath and dyspnea on exertion. A rating between 2+ and 3+ was assigned if the moderate shortness of breath and dyspnea on exertion were accompanied by mild (3 pillow) orthopnea. A 3+ severity corresponded with the progression of these symptoms to shortness of breath at rest; acute respiratory distress; dyspnea following minimal exertion, such as climbing one flight of stairs or walking a few steps to one block; frequent nocturia; and paroxysmal nocturnal dyspnea.

Radiographic change in the pulmonary vasculature was assigned at least 2+ to 3+ left ventricular dysfunction. Findings of this degree included increased vascularity, Kerley B lines, and controllable pleural effusions. Manifestations of 3+ severity consisted of unremitting pleural effusions and pulmonary edema which responded to treatment. The rating of 4+ was assigned to intractable pulmonary edema.

For right-sided congestive failure, a grade of 1+ indicated moderate jugular venous distention at an inclination of 45 degrees or less, or hepatomegaly with the liver edge palpable at one or two fingerbreadths below the right costal margin, but without overt edema. A value of 2+ was assigned for moderate jugular venous distention and hepatomegaly if minimal ankle or pretibial edema was also present. The severity was between 2+ and 3+ if, in addition to jugular venous distention and hepatomegaly, the edema was pitting in quality and extended to the knee, or if it involved both upper and lower extremities. Right ventricular failure of 3+ severity included jugular venous distention to the mandibular angle at 90 degrees, hepatomegaly ranging from 4 to 10 cm below the right costal margin, a positive hepatojugular reflux, ascites of cardiac origin, and pitting of the entire leg, with or without sacral edema. The 4+ rating was assigned for generalized anasarca. When central venous pressure (CVP) data were available, a level of 0 was assigned for a CVP of less than 15 cm H_2O; 1+ for 15–24 cm H_2O; 2+ for 25–34 cm H_2O; 3+ for over 35 cm H_2O. As for left-sided failure, the rating of right-sided congestive failure represented the combined information of many clinical features, and the presence of significant edema was necessary for a rating of 3+ or more. In the analysis of both left- and right-sided cardiac decompensation, values over 1+ or more represent those patients with a diagnosis of at least mild to moderate congestive failure. The duration of left- and right-sided heart failure was defined as the interval between the onset of symptoms of failure or the actual diagnosis of failure and the date of death.

The severity of hypotension during the terminal admission was graded according to the systolic pressures recorded in the clinical summaries and was classified as either sustained or episodic. A period over 1 hour was required for sustained shock. The terminal decline of blood pressure was not included in either the sustained or episodic category. Severity was classified as 0 for normotensive, 1+ for 90–99 mm Hg systolic, 2+ for 80–89 mm Hg, 3+ for 60–79 mm Hg, and 4+ for less than 60 mm Hg systolic. The duration of sustained shock in hours was noted. Episodic shock (lasting less than 1 hour) was graded as 0 for pressures ranging from normotensive to 100 mm Hg, 1+ for 90–99 mm Hg systolic, 2+ for 70–89 mm Hg, 3+ for 60–69 mm Hg, 3+ to 4+ for systolic pressures less than 60 mm Hg but without cardiac arrest, 4+ for ventricular fibrillation or asystole.

Fourteen pathologic variables, including body and organ sizes, cardiac chamber volumes and valve circumference, and histologic features in sections of liver, kidney, and adrenal, were examined. The histologic features were graded on a semiquantitative scale (0 to 4+). We identified chronic passive congestion and centrilobular necrosis on the basis of histologic changes. The features used to establish the presence of chronic passive congestion were atrophy of hepatic parenchymal cells, distention of sinusoids, and, in the severe grades, fibrosis, in the centrilobular areas (Figure 1). The presence of centrilobular necrosis was defined as necrosis of centrilobular hepatic parenchymal cells (Figure 2). In adrenals we determined the severity of two histologic features: cortical nodular hyperplasia and cortical medullary junction necrosis (Figure 3). Cortical nodular hyperplasia has a known association with hypertension, which was confirmed in our material, but there were no other significant correlations with manifestations of cardiac dysfunction. Cases with adrenal cortical medullary junction necrosis exhibited necrosis of variable numbers of cells, particularly involving the

zona reticularis. Recent studies have shown a correlation of this histologic finding with shock, an observation which was also confirmed in the present series.[4,5]

Sections of kidney were examined for the severity of acute tubular necrosis, a histologic finding associated with shock.[6] The histologic features in acute tubular necrosis are quite variable, depending upon the severity of insult and the elapsed time until death. We used three separate features in determining this diagnosis: actual necrosis of the renal tubular epithelium; dilatation of renal tubules with proteinaceous casts; and the accumulation of nucleated cells in the vasa recta.[7] All data were keypunched for computer processing and analyzed statistically by the use of Pearson's r coefficient and stepwise multivariate regression analysis.[8,9]

Results

One thousand adult autopsy subjects at The Johns CPC, no CLN or trivial CLN, and a mean liver weight amined. The patients ranged in age from 16 to 95 years (average 60 years), and 616 patients were male. The patient series included 409 with systemic hypertension, 203 with diabetes mellitus, 215 patients with angina pectoris, 187 patients with atrial fibrillation, and 435 patients with one or more myocardial infarcts. Table 1 shows the series of 1000 patients subdivided according to both chronic passive congestion (CPC) and centrilobular necrosis (CLN). A majority of patients (650/1000 = 65%) had CPC or trivial CPC, no CLN or trivial CLN, and a mean liver weight 1634 g. With increasing CPC there was a tendency for liver weight to decrease ($r = -0.12$, $P < 0.001$). Centrilobular necrosis was not correlated with liver weight.

In a statistical analysis of chronic passive congestion and centrilobular necrosis of the liver, distinct patterns of cardiac dysfunction emerged from the clinical and morphologic data. The correlation coefficients between chronic passive congestion and pathologic features for the entire group of patients

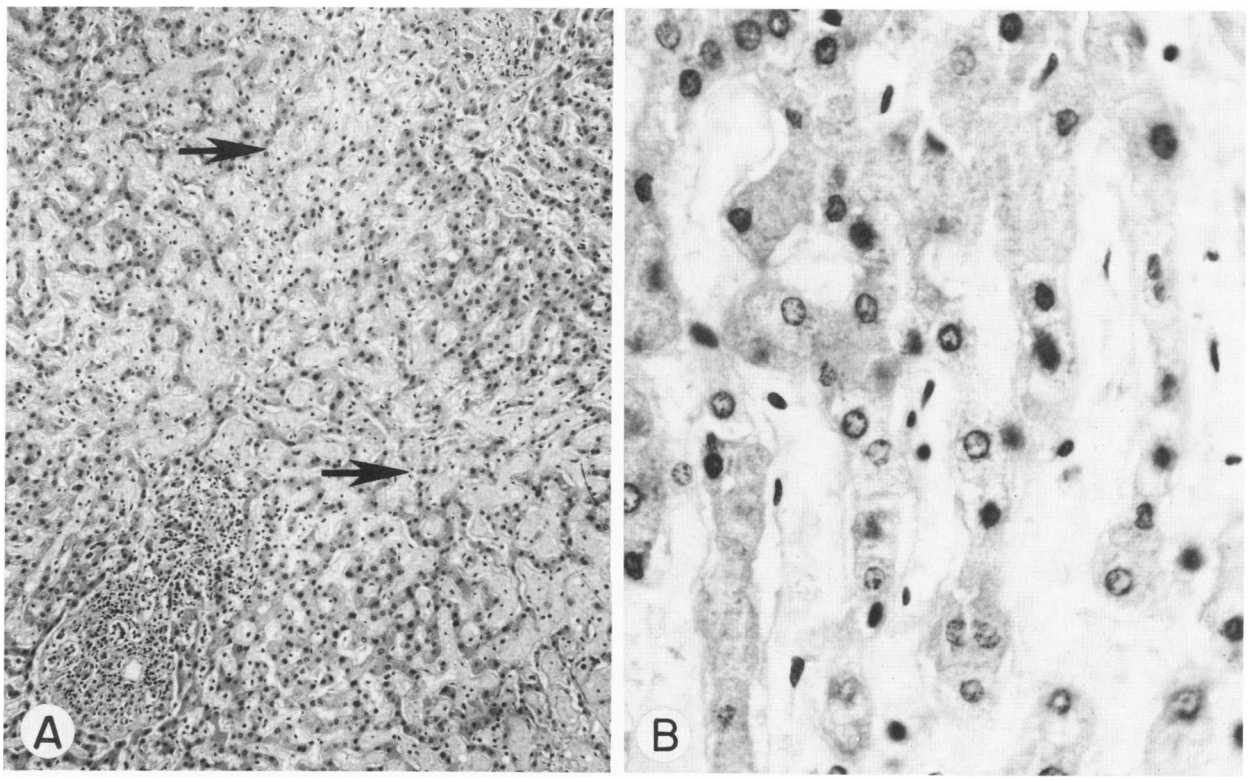

Figure 1 – Chronic passive congestion of the liver. **A** – The hepatic parenchyma surrounding the portal areas is well preserved, while that around the central veins (*arrows*) shows atrophy of the liver cell plates and dilatation of the sinusoids. (H&E, × 100) **B**—Junction of better preserved (*top*) and atrophic (*bottom*) parenchyma. In addition to sinusoidal dilatation, there is prominence of the space of Disse, which lies between the sinusoids and functions as a lymphatic. (H&E, × 600) (With a photographic reduction of 9%)

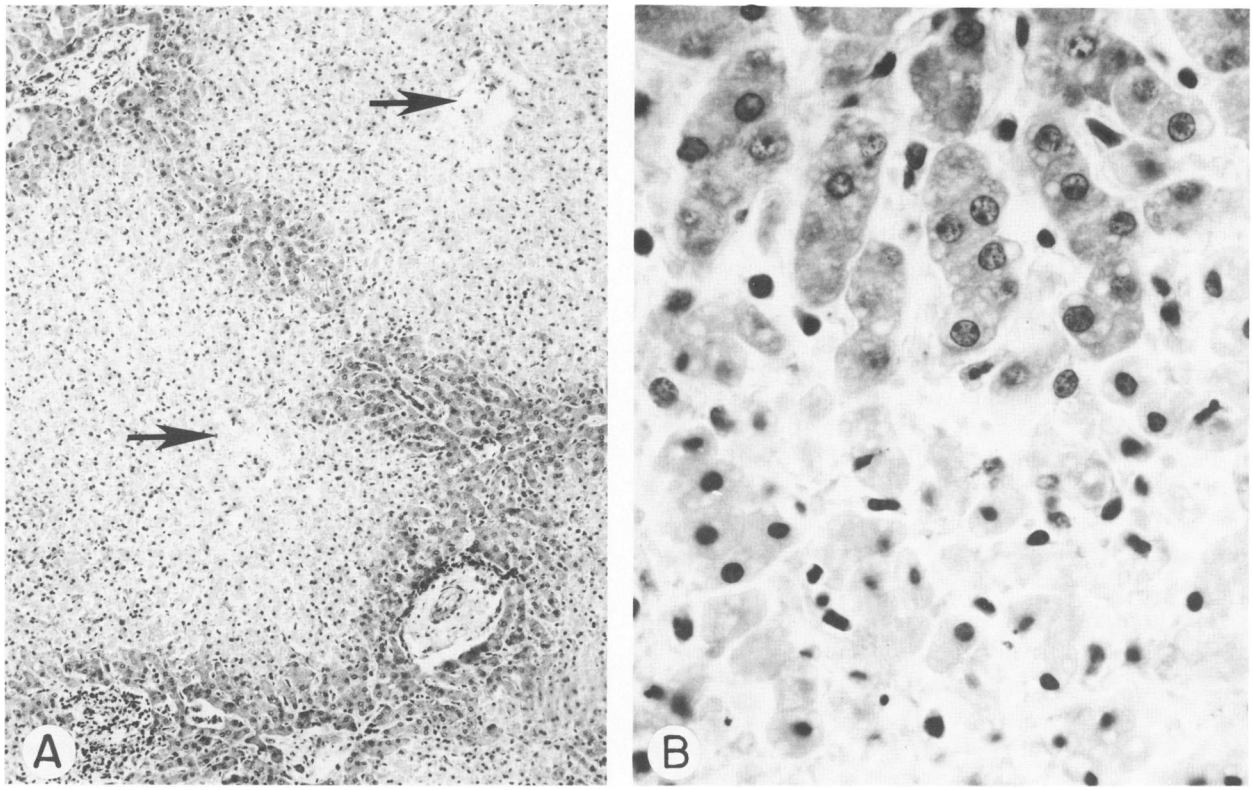

Figure 2—Centrilobular necrosis of the liver. **A**—The darker staining parenchyma around the portal areas is preserved. The majority of the tissue of the lobule surrounding the central veins (*arrows*) has undergone coagulation necrosis and stains pale. (H&E, × 100) **B**—Junction of preserved (*top*) and necrotic parenchyma (*bottom*). (H&E, × 600) (With a photographic reduction of 9%)

were significant at the 0.001 level for dilatation in all four cardiac chambers and for increased heart weight (Table 2). Chronic passive congestion also has a highly significant correlation with centrilobular necrosis, a fact that may tend to obscure some of the features associated with chronic passive congestion. We used a forward, stepwise multivariate regression analysis to determine which clinical variables would predict chronic passive congestion in the liver at the 0.001 level of significance (Table 3). In order to minimize the effect of associated centrilobular necrosis, we first analyzed the group of 786 patients with slight or no centrilobular necrosis (Table 1, column 1). Only one variable, the severity of right-sided congestive heart failure, entered the regression analysis. When all 1000 patients were analyzed and centrilobular necrosis was permitted to enter the list of dependent variables, again only one clinical variable, namely, right-sided congestive heart failure, entered the regression analysis as a predictor of chronic passive congestion, along with centrilobular necrosis. This clinical variable is associated with conditions producing elevated systemic venous pressure. As we shall see, centrilobular necrosis is associated with reduced arterial pressure.

The correlation coefficients between centrilobular necrosis and pathologic features for the entire group of patients were significant for adrenal cortical medullary junction necrosis ($P < 0.05$) and renal acute tubular necrosis ($P < 0.001$) (Table 4). The correlation coefficients for heart weight and chamber volumes compared with CLN were less than those compared with CPC, with the exception of left-ventricular volume. These adrenal and renal lesions have a known association with clinical shock, which was confirmed in our series of 1000 patients. Again, we observe the strong correlation between centrilobular necrosis and chronic passive congestion. We used multivariate regression analysis to determine which clinical variables would predict centrilobular necrosis in the liver at the 0.001 level of significance (Table 5). We first analyzed the group of 753 patients with slight or no chronic

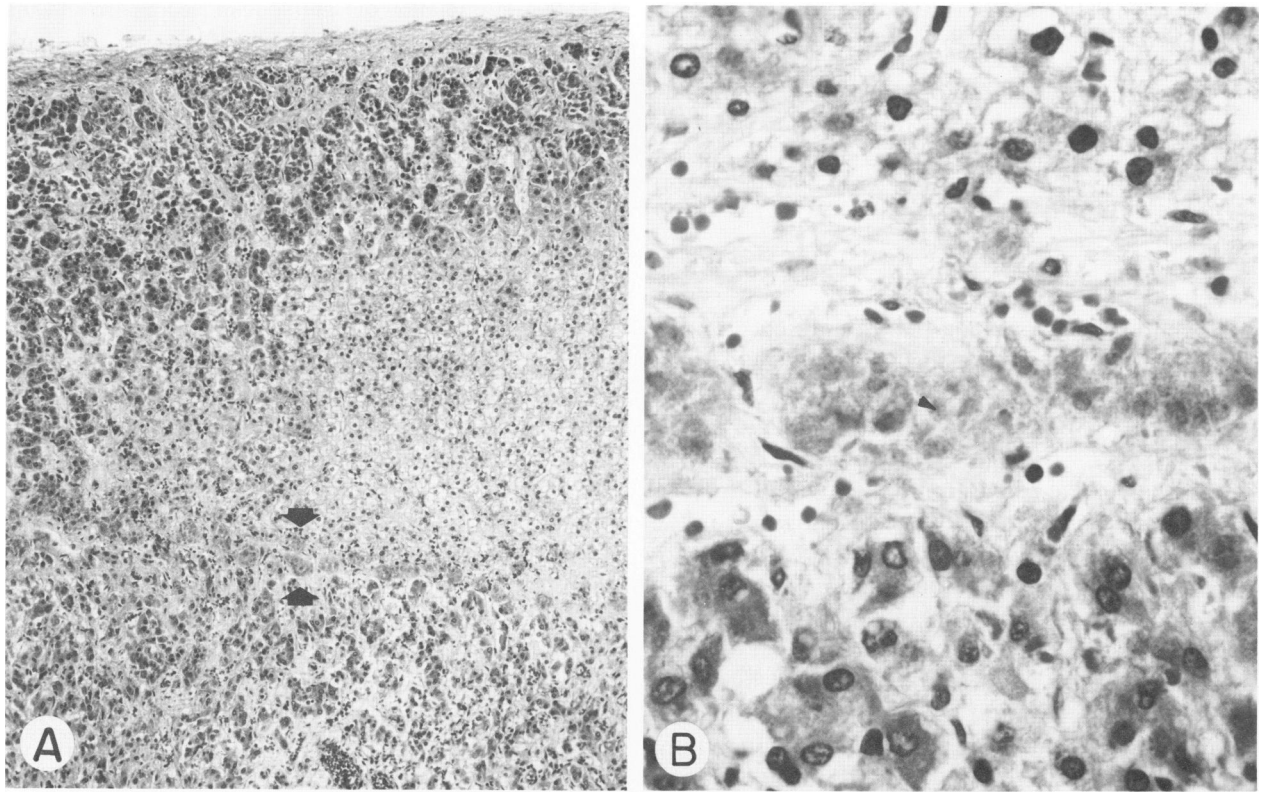

Figure 3—Adrenal corticomedullary junction necrosis. **A**—Cortex (*top*) and medulla (*bottom*) of an adrenal with a band of necrosis (*arrows*) in the zona reticularis adjacent to the medulla. (H&E, ×100) **B**—The zone of necrotic cells of the zona reticularis is in the middle, the preserved cortex is above, and the medulla is below. (H&E, ×600) (With a photographic reduction of 9%)

passive congestion (Table 1, row 1). Two variables, shock and renal failure, entered the regression analysis. When all 1000 patients were analyzed and chronic passive congestion was permitted to enter the list of dependent variables, the same two clinical variables, shock and renal failure, again entered as predictors of centrilobular necrosis, along with chronic passive congestion. The two clinical variables are associated with conditions producing reduced systemic arterial pressure, the pathologic variable with conditions producing elevated systemic venous pressure.

The results show that when the hepatic lesions are considered separately, chronic passive congestion arises from conditions producing elevated systemic venous pressure, whereas centrilobular necrosis arises from conditions producing reduced systemic arterial pressure. When the hepatic lesions are considered together, there is a highly significant association between chronic passive congestion and centri-

Table 1—Distribution of Liver Weights in 1000 Autopsy Subjects

Chronic passive congestion	Centrilobular Necrosis							
	None or trivial		Mild-moderate		Severe		Total	
	n	Liver wt*	n	Liver wt*	n	Liver wt*	n	Liver wt*
None or trivial	650	1634 ± 20	63	1631 ± 72	40	1731 ± 189	753	1639 ± 21
Mild-moderate	85	1503 ± 55	44	1439 ± 60	20	1359 ± 80	149	1465 ± 38
Severe	51	1593 ± 75	30	1167 ± 80	17	1477 ± 74	98	1519 ± 51
Total	786	1617 ± 19	137	1525 ± 44	77	1576 ± 102	1000	1601 ± 18

* Mean ± standard error, in grams.

Table 2—Correlation of Chronic Passive Congestion With Other Pathologic Variables in 1000 Subjects

	r	P<
Heart weight	0.25	0.001
Right atrial volume	0.28	0.001
Right ventricular volume	0.16	0.001
Left atrial volume	0.19	0.001
Left ventricular volume	0.12	0.001
Centrilobular necrosis	0.32	0.001

Table 4—Correlation of Centrilobular Necrosis With Other Pathologic Variables in 1000 Subjects

	r	P<
Left ventricular volume	0.14	0.001
Adrenal cortical-medullary junction necrosis	0.09	0.01
Acute tubular necrosis	0.15	0.001
Chronic passive congestion	0.32	0.001

lobular necrosis, suggesting that the presence of one may potentiate the other.

Discussion

Chronic passive congestion (CPC) and centrilobular necrosis (CLN) frequently appear together in the liver during cardiac dysfunction. However, the pathogenesis of these lesions in this situation is yet uncertain, particularly the factors responsible for CLN. In a recent review article, it was suggested that hypoxia sufficient to cause CLN can be generated by an increase in hepatic venous pressure.[1] CLN is associated with at least a moderate degree of hepatic congestion, and it is further suggested that perisinusoidal edema arising secondary to increased venous pressure may reduce oxygen diffusion to a critical level. Using 50% occlusion of the inferior vena cava, both CPC and CLN were produced, possibly duplicating the changes seen in clinical CHF.[10] However, the assumption that the pressures obtained by such manipulations are representative of central venous pressure in clinical CHF has been questioned. In fact, there is a lack of correlation between right atrial pressure and the amount of hepatocellular necrosis.[11] The capacity of prolonged CPC in RCHF to produce CLN has been claimed without supporting pathologic data.

Hypoxia in the centrilobular areas can also be created by diminished hepatic perfusion, but there is disagreement as to what level of hypoperfusion is required in order to exceed hepatic oxygen extraction. Some authors suggest that the addition of fever or exercise in a setting of CPC is sufficient to precipitate CLN.[1] Others have considered the most frequent etiology of hepatocellular necrosis linking central veins as "congestive heart failure,"[12] implying that the extent of hypoperfusion should correlate with diminished cardiac output. In contrast, Sherlock[11] has noted the lack of a significant correlation between lowered cardiac output and the extent of centrilobular necrosis. In summary, the frequent appearance of CLN in cases of cardiac dysfunction is evidence for circulatory alterations producing a lowered oxygen tension. Hypoxia sufficient to produce CLN is thought to be adequately explained by the contributions of CPC or low cardiac output, or both.

The present study of 1000 autopsy subjects demonstrates that hypoxia sufficient to produce CLN requires the presence of shock. Centrilobular necrosis, occurring regardless of the presence of CPC, correlates significantly ($P < 0.001$) with the severity of sustained or episodic hypotension in the patient's course. Similarly, clinically evident renal failure, often precipitated by shock, is also a strong predictor of hepatic CLN. Pathologically, CLN is associated with adrenal cortical medullary junction necrosis (CMJN) ($P < 0.01$) and renal acute tubular necrosis (ATN) ($P < 0.001$). While shock as a cause of renal ATN has been established, the recognition of hypotension as the cause of CMJN is a more recent devel-

Table 3—Prediction of Chronic Passive Congestion of the Liver by Multivariate Regression Analysis

Clinical variables* in 786 patients with slight or absent centrilobular necrosis
CPC (0-4+) = 0.21
+ 0.33 RCHF (0-4+) SE = 0.33 r = 0.47

Centrilobular necrosis and clinical variables* in all 1000 patients
CPC (0-4+) = 0.17
+ 0.36 RCHF (0-4+) SE = 0.03
+ 0.24 CLN (0-4+) SE = 0.03 r = 0.52

* Entered to a significance level of $P < 0.001$.

Table 5—Prediction of Centrilobular Necrosis of the Liver by Multivariate Regression Analysis

Clinical variables* in 753 patients with slight or absent chronic passive congestion
CLN (0-4+) = 0.14
+ 0.09 Shock (0-4+) SE = 0.02 r = 0.25
+ 0.32 Renal Failure SE = 0.07
(0 = No, 1 = Yes)

Chronic passive congestion and clinical variables* in all 1000 patients
CLN (0-4+) = 0.13
+ 0.11 Shock (0-4+) SE = 0.02
+ 0.30 Renal Failure SE = 0.06
(0 = No, 1 = Yes)
+ 0.28 CPC (0-4+) SE = 0.03 r = 0.41

* Entered to a significance level of $P < 0.001$.

opment.[4,5] It should be emphasized that while shock and renal failure are correlated with CLN, clinically defined left-sided congestive failure does not predict CLN.

As indicated above, the assignment of shock as the cause of CLN arising during congestive failure is not described in the recent literature but is mentioned in earlier reports. One investigation of serum transaminase levels concluded that venous hypertension alone, without a decrease in blood pressure, was not associated with acute central necrosis of the liver.[13] This confirmed other findings that CLN was independent of the severity and duration of CHF without superimposed shock.[14-16] These reports all emphasize the predominant role of shock in the etiology of hepatic CLN.

Hepatic CPC, on the other hand, is associated with elevated systemic venous pressure. If considered separately from CLN, CPC is correlated ($P < 0.001$) with right-sided, but not with left-sided, congestive heart failure. In left-sided failure, venous hypertension is limited to the pulmonary vasculature. The association between RCHF and hepatic CPC is well established.[11,17,18] Prediction of CPC by atrial fibrillation when all 1000 patients were considered is explained by the fact that atrial fibrillation is frequently seen in conditions eventually producing right-sided failure, including rheumatic mitral stenosis and coronary artery disease.[19] Among the pathologic variables, correlations exist ($P < 0.001$) between CPC and gross increases in heart weight and cardiac chamber volume. These are consistent with clinical decompensation and reinforce the association of elevated venous pressure and hepatic CPC.

The correlation in 1000 patients between CLN and shock and between CPC and elevated venous pressure are at variance with other reported series.[20,21] In patients with CLN, there was no evidence of hypotension (or RCHF) at presentation. Biopsies revealed significant numbers of erythrocytes accompanying the CLN and replacing hepatocyte cords. This lesion histologically has been associated with elevated venous pressure, as it has been noted in experimental venous occlusion,[22,23] Jamaican veno-occlusive disease,[24,25] the Budd-Chiari syndrome, and hepatic vein thrombosis with other causes.[26] Because varying degrees of left-ventricular decompensation were present in these patients, it was concluded that LCHF was the cause of the CLN. Elevated serum transaminase levels in these patients were cited in support of this pathogenesis, increases in SGOT levels having previously been reported in cases of myocardial injury[13]; however, these levels were uniformly associated with significant hypotension, which was absent in these patients. LCHF as the appropriate cause of the CLN in these reports is controversial at the present time.

While CPC and CLN have distinct hemodynamic causes when considered separately, they frequently occur together. The correlation coefficient analysis indicates that the presence of one lesion predicts the other ($r = 0.32$, $P < 0.001$). This suggests that although the origins of CPC and CLN may be different, the local alterations resulting from one lesion may enhance pre-existing morphologic features of the other. CPC may contribute to the development of the morphologic features of CLN, exacerbating the effect of a depressed arterial pressure. Hepatocellular atrophy and stagnation of sinusoidal flow may predispose the centrilobular region to necrosis. In addition, Safran and Schaffner[27] have demonstrated the active deposition of perisinusoidal collagen in CPC. CLN, on the other hand, may potentiate the local effects of elevated venous pressure. Congestion of the sinusoids and central vein frequently accompany necrosis, although there may be little or no inflammatory response.[28] Some authors[14] have regarded this concomitant congestion as a criterion for CLN. Secondly, the accumulation of stromal connective tissue following hepatic necrosis, in contrast to CPC, occurs by both passive reticulin condensation as well as active deposition.[29] This reciprocal potentiation between CPC and CLN, based on local effects of the lesions, may account for the frequency of their simultaneous appearance in cardiac dysfunction.

Chronic passive congestion and centrilobular necrosis are the pathologic manifestations of distinct systemic vascular conditions. Statistical analysis of 1000 patients permitted a separation of the two lesions. CLN was associated with shock and with clinical and pathologic sequelae of hypotension, but not with left-sided CHF. CPC was associated with right-sided CHF and other conditions producing elevated systemic venous pressure. Among the entire group of patients, however, an association exists between CPC and CLN. This indicates that local alterations resulting from one lesion may enhance the underlying pathologic features of the other lesion.

References

1. Dunn GD, Hayes P, Breen KJ, Schenker S: The liver in congestive heart failure: a review. Am J Med Sci 1973, 265:174–189
2. Zimmerman HM, Hillsman JA: Chronic passive congestion of the liver: An experimental study. Arch Pathol 1930, 9:1154–1163
3. Hutchins GM, Anaya OA: Measurements of cardiac size, chamber volumes and valve orifices at autopsy. Johns Hopkins Med J 1973, 133:96–106

4. Kuhajda FP, Moore GW, Hutchins GM: Adrenal insufficiency secondary to massive corticomedullary junction hemorrhage following hypotension in three anticoagulated patients. Circ Shock 1978, 5:291-297
5. Kuhajda FP, Hutchins GM: Adrenal cortico-medullary junction necrosis: A morphologic marker for hypotension. Am Heart J 1979, 98:294-297
6. Heptinstall RH: Pathology of the Kidney. 2nd edition. Boston, Little, Brown, 1974, pp 781-820
7. Solez K, Morel-Maroger L, Sraer JD: The morphology of "acute tubular necrosis" in man: Analysis of 57 renal biopsies and a comparison with the glycerol model. Medicine 1979, 58:362-376
8. SAS User's Guide—1979 Edition. SAS Institute, Inc., Raleigh, 1979, pp 237-263
9. Draper NR, Smith H: Selecting the "best" regression equation, Applied Regression Analysis. New York, John Wiley & Sons, 1966, pp 163-216
10. Sherlock S: The liver in circulatory failure, Diseases of the Liver. 4th edition. Edited by L. Schiff. Philadelphia, J. B. Lippincott Company, 1975, pp 1033-1050
11. Sherlock S: The liver in heart failure: Relation of anatomical, functional, and circulatory changes. Br Heart J 1951, 13:273-293
12. Buhac I, Agrawal AB, Park SK, Lomotan A, Lowen B, Balint JA: Jaundice and bridging centrilobular necrosis of liver in circulatory failure. NY State J Med 1976, 76:678-682
13. Killip T III, Payne MA: High serum transaminase activity in heart disease: Circulatory failure and hepatic necrosis. Circulation 1960, 21:646-660
14. Ellenberg M, Osserman KE: The role of shock in the production of central liver cell necrosis. Am J Med 1951, 11:170-178
15. Clarke WTW: Centrilobular hepatic necrosis following cardiac infarction. Am J Pathol 1950, 26:249-255
16. Lambert RA, Allison BR: Types of lesion in chronic passive congestion of the liver. Johns Hopkins Hosp Bull 1951, 27:350-356
17. White TJ, Wallace RB, Gnassi AM, Kemp NF, Price HP, Leevy CM: Hepatic abnormalities in congestive heart failure: Needle biopsy studies. Circulation 1951, 3:501-507
18. Katzin HM, Waller JV, Blumgart HL: "Cardiac cirrhosis" of the liver: A clinical and pathologic study. Arch Int Med 1939, 64:457-470
19. Marriot HJL, Myerburg RJ: Recognition and treatment of cardiac arrhythmias and conduction disturbances, The Heart, Arteries and Veins. (Hurst JW, ed), 4th edition. Edited by JW Hurst. New York, McGraw-Hill Book Company. 1978, pp 637-694
20. Cohen JA, Kaplan MM: Left-sided heart failure presenting as hepatitis. Gastroenterology 1978, 74:583-587
21. Kanel GC, Ucci AA, Kaplan MM, Wolfe HJ: A distinctive pericentral liver lesion associated with heart failure. Am J Clin Pathol 1980, 73:235-239
22. Bolton C, Barnard WG: The pathological occurrences in the liver in experimental venous stagnation. J Pathol Bacteriol 1931, 34:701-709
23. Leopold JG, Parry TE, Storring FK: A change in the sinusoid-trabecular structure of the liver with hepatic venous outflow block. J Pathol 1970, 100: 87-98
24. Bras G: Aspects of hepatic vascular diseases, The Liver. Edited by EA Gall, FK Mostofi. Baltimore, Williams and Wilkins 1973, pp 406-430
25. Brooks SEH, Miller CG, McKenzie K, Audretsch JJ, Bras G: Acute veno-occlusive disease of the liver: Fine structure in Jamaican children. Arch Pathol 1970, 89:507-520
26. Reynolds TB, Peters RL: Budd-Chiari syndrome,[10] pp 1402-1411
27. Safran AP, Schaffner F: Chronic passive congestion of the liver in man: Electron microscopic study of cell atrophy and intralobular fibrosis. Am J Pathol 1967, 50:447-463
28. Cook GD: Hepatic changes associated with shock. Int Anesthesiol Clin 1969, 7:883-894
29. Popper H: Pathological aspects of cirrhosis: A review. Am J Pathol 1977, 87:228-264