# CENTRILOBULAR HEPATIC NECROSIS FOLLOWING CARDIAC INFARCTION*

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This is a report on the incidence and morphologic features of centrilobular necrosis of the liver following myocardial infarction.

Centrilobular necrosis is a common finding at autopsy. It has been described in such conditions as trauma, postoperative shock, the crush syndrome, burns, infections, blackwater fever, anaphylaxis, high-altitude flying, and experimental shock.[1] It probably has been overlooked following myocardial infarction because it may be obscured by, and confused with, the changes of congestive heart failure.

The present study is based on the autopsy records of all cases of myocardial infarction of less than 6 weeks' duration in the files of the Banting Institute in the 5-year period ending June, 1948. There were 61 cases in 1793 autopsies. Fifty autopsies from the same period without myocardial infarction, but in which congestive heart failure was diagnosed either clinically or at autopsy, were reviewed as controls. Nine of the cases of infarction had typical centrilobular hepatic necrosis, whereas this was found in only one of the control cases.

Application of the $\chi^2$ test to these results shows that they would occur less than once in twenty times by chance and they are therefore considered significant.[2]

## HISTOLOGIC CHANGES

The earliest lesions seen consisted of dissociation of the hepatic cells in the centrilobular areas with pyknosis of their nuclei. There was increased eosinophilia of the cytoplasm with little or no shrinkage or swelling. This gave the necrotic areas in the liver a loss of structure and change in color so that they were easily picked out with the low power of the microscope (Figs. 1 and 2). This change occurred less than 24 hours after myocardial infarction, which is in agreement with its time of development in the crush syndrome.[3] The lesions usually surrounded the central veins, but sometimes extended to become almost confluent. In other cases they involved only segments beside central veins, and some lesions appeared mid-zonal, although this may have been due to their being cut in a plane that missed the adjacent vein. In some cases hemorrhage had occurred in the necrotic areas, making them difficult to distinguish from the changes of passive congestion. In the next 5 days the lesions were rapidly surrounded

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and infiltrated by polymorphonuclear leukocytes. The nuclei of the hepatic cells disappeared, their cytoplasm lost its outlines and began to disintegrate (Fig. 3). There were not sufficient cases in the series to time the progress of the lesions accurately.

In a few of the sections there was patchy lipidic vacuolation of the liver cells in the necrotic areas. This vacuolation had probably been present before the infarction. These cells were not so rapidly absorbed, for their outline containing the fat droplet persisted in the otherwise empty stroma (Fig. 4).

When the dead liver cells were absorbed, there remained sinusoids filled with blood, and the lesions then became indistinguishable from those of passive congestion.

The reticulin fibers in the areas of necrosis were not destroyed, and apparently the liver cells may be quickly regenerated to form normal liver. Examination of these cases and many others in which death occurred longer than 6 weeks after the myocardial infarction showed no evidence of permanent lesions that could have resulted from centrilobular necrosis. In the presence of heart failure, however, regeneration of liver tissue did not occur.

In the controls, the well known congestion and centrilobular atrophy and degeneration of chronic venous congestion were frequently found. In the most advanced stage of this, there might be a few necrotic liver cells and some associated polymorphonuclear infiltration, but these inflammatory cells were never focal. Perhaps necrosis of liver cells in such cases is due to the high degree of circulatory failure that may exist for a few hours before death. It can be distinguished by the gradual atrophy and degeneration of the liver cell columns as they approach the central vein. It is most marked in cases of cor pulmonale. The hepatic lesions in chronic passive congestion have been well described by Lambert and Allison.[4] One of their five types of lesions was centrilobular necrosis identical with that described here as being due to myocardial infarction and not to congestive failure. It is significant that the two examples they give for this group are both obvious cases of recent myocardial infarction, their case 9 being proved such by autopsy. It is a common error to attribute these necrotic lesions to congestive failure rather than to myocardial infarction and the associated shock. In the one control case with typical centrilobular necrosis of the liver there was adequate explanation in the lungs for the hepatic lesions on the basis of anoxia. The left lung consisted of fibrous tissue and bronchiectatic cavities and sank in

water. The right weighed 1330 gm. and the functioning parenchyma was largely emphysematous or replaced by tuberculous consolidation and cavitation. The same hepatic lesion has been seen in lobar pneumonia when large parts of the lungs were involved and there was no cardiac failure.

## Clinical Data

Data relating to the 9 cases with necrosis of the liver are summarized as follows:

| Case no. | Age and sex | Age of infarct at death; clinical and microscopic | Weight of heart | Blood pressure before infarction | Blood pressure at time of infarction |
|---|---|---|---|---|---|
| | *yrs.* | | *gm.* | *mm. of Hg* | *mm. of Hg* |
| 1 | M 62 | 7 hours | 330 | 190/105 | 80/50 |
| 2 | M 61 | 19 hours | 400 | 170/110 | Not obtainable |
| 3 | F 44 | About 24 hours | 725 | 200/120 | 80/60 |
| 4 | M 68 | 2 days | 457 | 150/90 | 170/105 |
| 5 | M 52 | 6 days | 860 | ? | 74/55 |
| 6 | F 41 | About 14 days | 520 | 210/140 | ? |
| 7 | M 73 | 18 days | 485 | ? | "Low" |
| 8 | M 68 | 3 weeks | 350 | 250/130 | 130/90 |
| 9 | M 45 | 4 weeks | 415 | 185/100 | ? |

In 6 of the cases with typical hepatic necrosis the patients died within 2 weeks of the myocardial infarction, and it is in this interval that necrosis should be most common. The cases in which death occurred 18 days and 4 weeks after the myocardial infarction had embolic complications, and the patient dying 3 weeks after the infarction continued to have pain in this interval. The lesions in these cases were characteristic, and it is probable that they were due to some circulatory disturbance occurring after the original infarct.

Clinically, shock was commented upon in 5 of the cases with centrilobular hepatic necrosis. This was more frequent than in the cases of myocardial infarction without necrosis of the liver. The other factor that appeared to be significant was hypertension. This was marked in 3 cases, present in 3, and suggested in 2 others by the cardiac hypertrophy in the absence of valvular disease. It would seem reasonable that the decrease in hepatic arterial blood supply would be greater when the fall in blood pressure was greater, and the peripheral resistance of the circulatory system increased.

## Discussion

The cause of the liver necrosis is probably acute anoxia due to shock occurring at the time of the myocardial infarction. The differ-

ences between this lesion and the changes in passive congestion have been pointed out in detail. The development of necrosis is not dependent on congestive heart failure, for it occurred in cases in which there was no evidence of heart failure either clinically or at autopsy. Other explanations for these lesions in shock have been offered. A conditioning nutritional factor has been suggested by Himsworth.[5] He has suggested also that swelling of the peripheral cells of the lobule may shut off the circulation to the centrilobular cells in carbon tetrachloride poisoning in animals,[6] but in shock in general and in my cases in particular the peripheral cells in the lobule appear normal at all stages and there is no clinical or pathologic evidence of portal obstruction at any time. Maegraith's theory[7] that similar lesions in blackwater fever are due to valves in the hepatic veins causing back pressure is based chiefly on evidence from dogs, in which such valves are prominent and the liver is one of the organs most affected by shock. Centrilobular necrosis does not occur in experimental obstruction of the inferior vena cava,[8,9] nor in spontaneous obstruction of the hepatic veins in man.[10] The theory that the liability to damage of the center of the lobule depends on a progressive fall in oxygen tension in the blood traversing the sinusoids has yet to be disproved, and would explain the distribution of necrosis in conditions of circulatory failure and collapse.

## Summary

Focal necrosis in the liver following cardiac infarction presents characteristic morphologic features. It is to be differentiated from the changes of passive congestion.

It was found in 9 of 61 consecutive autopsies with recent myocardial infarction.

The lesions are recognizable in the first 2 weeks following cardiac infarction, and disappear within 1 month leaving no permanent hepatic changes.

They are the same as the hepatic lesions found in shock from any cause, and are believed to be due to acute anoxia.

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[ *Illustrations follow* ]

## DESCRIPTION OF PLATE

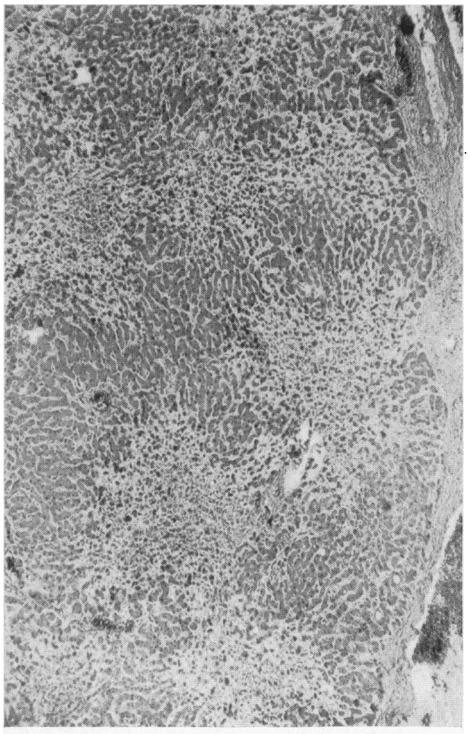
### PLATE 42

FIG. 1. Early centrilobular necrosis. × 40.

FIG. 2. Higher magnification of one of the lesions in Figure 1 showing cell dissociation and necrosis. × 300.

FIG. 3. A later stage of necrosis with infiltration of polymorphonuclear leukocytes. × 180.

FIG. 4. Higher magnification of a portion of Figure 3. The vacuolated liver cells remain although normal cells have been absorbed. × 300.



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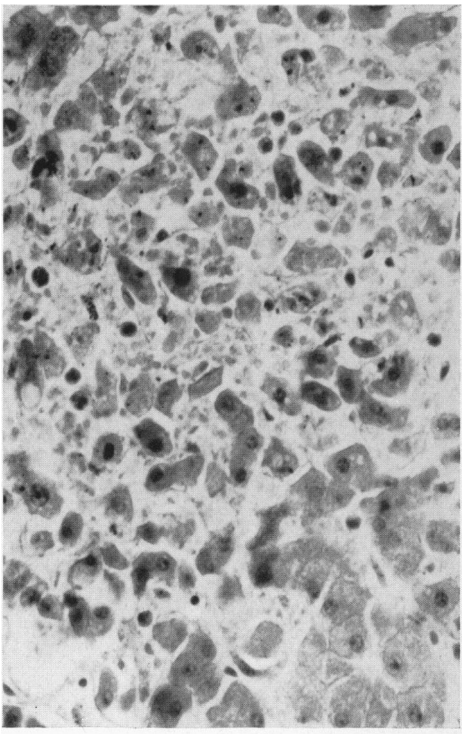

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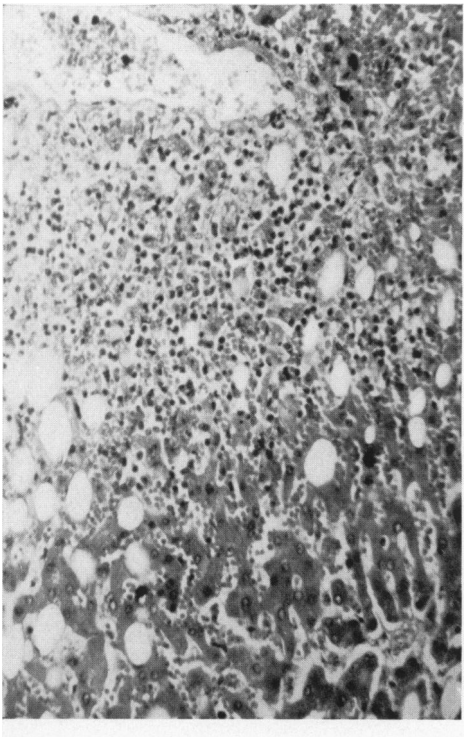

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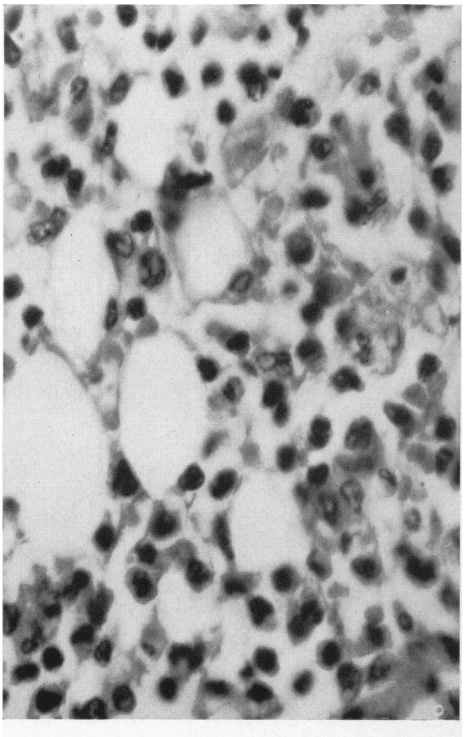

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Clarke

Centrilobular Hepatic Necrosis