

Long-term Studies on the Therapy of Hepatic Damage and Cirrhosis of Liver

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The liver plays a major role in the nutrition and maintenance of the body as it dominates the intermediary metabolism by which food stuffs, after absorption, are finally prepared for assimilation and metabolism by the tissues. From the anatomical point of view, it is a receiving depot as well as a storehouse and chemical factory. Proper functioning of the liver has a significant effect on the physiological function and maintenance of a normal state of health.

Physiological Considerations

The concept of lobular architecture of the liver has been firmly established as a convenient unit of reference. The hepatic cells, which constitute the lobules may look identical in histological sections and yet they may be very different in functional activity (Novikoff). On one side of each hepatic cell is the sinusoid concerned with absorption and on the other side is the bile canaliculus concerned with secretion. The lining of the sinusoid formed of reticulo-endothelial Kupffer cells is separated from the hepatic cells by a potential space into which innumerable microvilli project and they enormously increase the absorptive surface of the cell. Similar micro villi are present on the canalicular side. On the canalicular surface there are adenosine triphosphatase and 5-nucleotidase but on the sinusoid surface there is only 5-nucleotidase. On either side of the bile canaliculus the cytoplasm is rich in acid phosphatase and golgi apparatus. This enzymatic differentiation of the secretory and absorptive surfaces of the cell, probably has important physiological significance (Novikoff).

Biochemical cytology technique reveals that as regards enzymatic activity, the lobule is heterogenous rather than homogenous. This supports the concept that heterogeneity of enzyme distribution may be the basis of the selective localisation of the lesions in the hepatic lobule due to poisons, toxins, infective agents, etc. A large number of agents - bacteria, viruses, toxins, drugs, chemicals, immune reactions, etc. - have been observed to damage the liver structure and/or function. Though our present-day knowledge is comparatively more accurate and precise, the degree of correlation between the structure and functions of the liver remains undefined. No satisfactory correlation can be shown either, between the clinical condition observed in patients with this disorder and the findings obtained from a host of biochemical and laboratory tests and even careful biopsy studies, to determine the degree and extent of liver damage.

Hepatic Necrosis and Damage

Hepatic necrosis may be diffuse, zonal or focal. Zonal necrosis may be central, midzone or peripheral, depending on the damaging agent and various other factors. The causes of hepatic necrosis may be many and varied. Variability of the causative factors is one of the chief reasons for the complexity of our understanding of its genesis today. The liver is unique in that 80% out of the blood it receives is venous in character. Consequently, hepatic cells in comparison with other cells in the body, are always living on the dangerous edge of things, for they exist in a condition of

partial anoxia. The characteristic reaction of the liver cells to an injurious agent is necrosis, which may be labelled with equal truth as either, hepatic necrosis or hepatitis. The liver has great reserve powers and it certainly does not work at full capacity at any time. No organ has greater power of cellular regeneration than the liver. When the injury is slight and transient, the dead cells are quickly removed and replaced by new liver cells. When it is severe or prolonged, there is likely to be proliferation of fibroblasts resulting in fibrosis which may be localised or generalised (which we call cirrhosis). These two processes are closely interwoven as inflammation and repair.

Liver Function and Biopsy Studies

Knowledge of normal liver function enables us to study the results of disturbed liver function. Observations on the behaviour of liver enzymes in the blood and a battery of liver function tests have provided information of marked value. Transthoracic aspiration biopsy of the liver is proving itself as useful in its own way as many of the functional tests. Its potential value, indeed, seems to be unlimited. It can be of immense value to the physician in his study and assessment of any disease process or therapy. It can also give him insight into the metabolic activities of the liver, it can throw light on the progress of disease and give guidelines for the effect of therapy. It also helps in estimating enzymatic activity, lipid utilisation and vitamin A content, etc. Fresh fields are likely to be opened up continually with advances in histochemical methods. The small size of the biopsy specimen is not as great a drawback as might be supposed, for, so many of the puzzling disease conditions of the liver are characterised by diffuse lesions and even localised lesions like sarcoidosis can be picked up in a surprising number of cases by liver biopsy. Enzymatic differentiation of the secretory and absorptive surfaces of the cell probably has important physiological significance. The hepatic lobule, as revealed by the technique of biochemical cytology is heterogenous rather than homogenous in enzymatic activity though the cells in the different parts of the lobule look alike. No satisfactory correlation can be shown, either, between the clinical condition observed in patients with the disorder and the findings obtained from a host of biochemical and laboratory tests, and even careful biopsy studies, to determine the degree and extent of liver damage. Once the diagnosis has been established, all that one can expect, hopefully, is to get functionally the best out of the remaining healthy or less affected hepatic parenchymatous cells towards its total function. This is because no substance is known to convert interstitial tissue again into a parenchymatous one. However, since the regenerative power and the functional reserves of the liver are very high, this becomes very significant from the clinical point of view. The lesions vary greatly in severity and the same is true of the symptoms. On needle biopsy examination, the lesions may be found to be diffuse or zonal. The diffuse ones heal rapidly and completely, but when the disease runs a longer course, there may be residual fibrosis in the portal zone after apparent clinical recovery.

Indian Childhood Cirrhosis

The main problem that confronts one in paediatric practice in India today and probably baffles us all is cirrhosis of the liver, known popularly as Indian Childhood Cirrhosis, or infantile cirrhosis of liver. The disease is met with mostly between the ages of 6 months and 3 years with a maximum incidence between one and three years. Once the diagnosis has been established, modern methods of therapy seem to offer poor prognosis. A cure of this disease is a standing challenge to our profession. Once the disease has developed and progressed, it is recognised that, search for its cure is futile. All that one could hope for is to get functionally the best out of the remaining less damaged or healthy liver parenchyma. Below is presented the report of a study of a case of established Indian Childhood Cirrhosis, which improved remarkably and showed clinical, biochemical and histopathological response. This observation seems to be a land-mark in the therapy of this problematic disease.

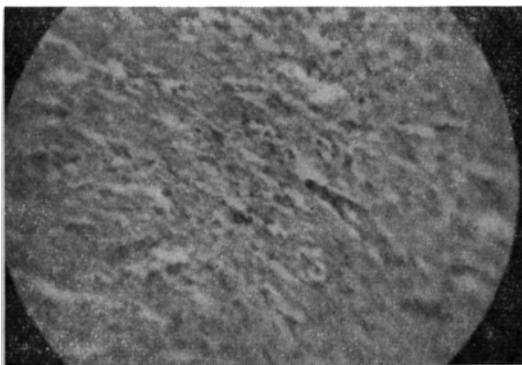
Reviewing the published clinical reports and histopathological studies, Mathur (1957), Captain S.R. and Sayed A.H. (1966), Joglekar, Chitale and Balwani (1963), Sheth, *et al.*, (1960), Patel, Jal

(1963), Joglekar and Leevy (1970), Liv.52 has showed marked protective action on the liver against hepatotoxic agents. Sule and Sathe reported functional and clinical improvement after Liv.52 therapy. The exact aetiology of cirrhosis of the liver is very elusive. Probably it is the end result of many processes, which bring about a change in the structure of the liver, which is altered and modified by these various processes.

Case Report and Observations

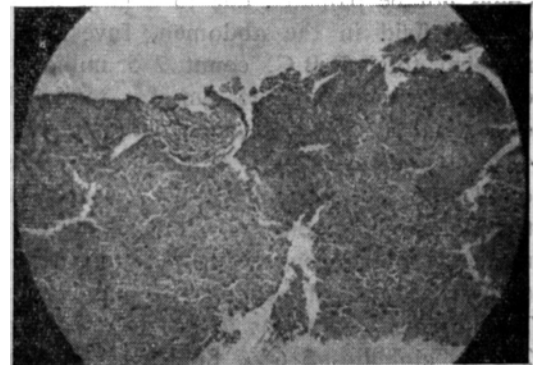
Dhijendra, 12 years old, male, came under our observation with a picture of advanced cirrhosis of the liver. His clinical picture revealed anaemia, mild jaundice with sunken cheeks, generalised anasarca with prominent veins all over the abdomen. The liver and spleen could not be palpated due to a large amount of free fluid in the abdomen. Investigations revealed total R.B.C. count 2.5 million per cmm. Haemoglobin 7.5 gm%, total white cell count 12,500 per cmm with Polymorph 48%, Lymphocytes 44%, Monocytes 4%, Eosinophil 4% and Basophil 0%. Urine showed trace of albumin, bile salts, bile pigments and normal urobilinogen; there were no deposits or casts. Stools showed ova of round worms. Total plasma proteins 5.8 gm%, albumin 2.2%, globulin 3.6%. SGPT 40 units. Initial liver biopsy showed cellular infiltration and loss of normal architectural pattern and evidence of fibrosis (vide photomicrographs I, II and III). He was put on Liv.52 drops one teaspoonful twice daily, a fairly large dose, besides the routine general treatment. Within a fortnight of the institution of therapy, the boy showed signs of improvement, the appetite improved, oedema of legs became gradually improved, oedema of legs became gradually less and disappeared, ascites

*PHOTOGRAPH I
Before Liv. 52 therapy*



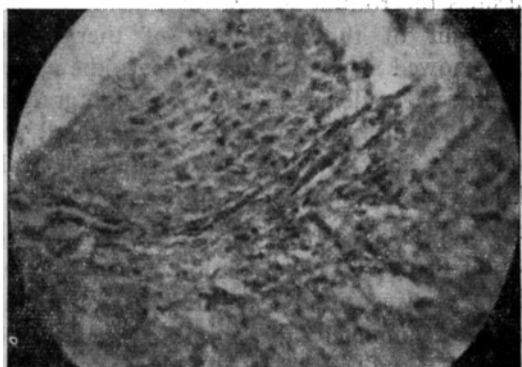
Cellular infiltration

*PHOTOGRAPH II
Before Liv. 52 therapy*



Loss of normal architectural pattern

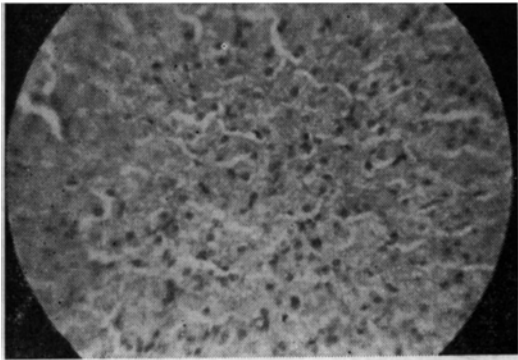
*PHOTOGRAPH III
Before Liv. 52 therapy*



Evidence of fibrosis

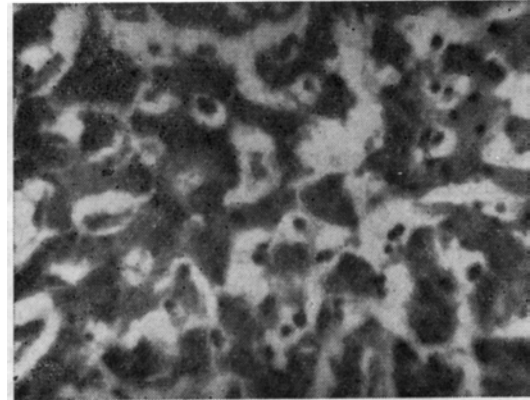
decreased considerably and it was now possible to feel a firm liver 2.5 cm below the costal margin in the midclavicular line spleen 1" below the left costal margin. After a period of three months from the institution of Liv.52 oral therapy, ascites completely disappeared. Anaemia improved considerably. The laboratory findings showed: Blood: Red blood cells 4.2 million per cmm, haemoglobin 10.6 gm%, total plasma proteins 6.4 gm%, albumin 3.4 gm% and globulin 3.0 gm%. Repeat liver biopsy after the therapy for three revealed evidence of regeneration of the liver cells, with absence of cellular infiltration and return of the hepatic architectural pattern to normal in scattered areas (vide photomicrographs IV and V). He is being regularly followed up and has shown remarkable clinical, biochemical and histopathological

PHOTOGRAPH IV
After Liv. 52 therapy



Regenerating Liver cells.
Cellular infiltration — Nil
Architectural pattern — evidence at

PHOTOGRAPH V
After Liv. 52 therapy



Showing cellular regeneration.
The duplicate nuclei are clearly seen.

improvement. Now he is receiving ½ teaspoonful Liv.52 drops twice daily for one year and is free from all signs and symptoms and completely normal.

SUMMARY

Twelve years old male child suffering from cirrhosis of the liver has been treated with very large doses of Liv.52 drops over a period of six months. Therapy showed significant clinical, biochemical and histopathological improvement which has continued during one year and he is completely normal.

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