THE EFFECTS OF MOUSE HEPATITIS VIRUS TYPE 3 ON THE MICROCIRCULATION OF THE LIVER IN INBRED STRAINS OF MICE

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Mouse Hepatitis Virus Type 3 (MHV-3) infection results in strain dependant liver disease. The acute effects of MHV-3 on the in vivo microcirculation of the liver in fully susceptible (Balb/cJ), fully resistant (A/J) mice and the chronic effects on C3H mice were studied. In Balb/cJ mice by 6 to 12 hours following infection, granular flow and sinusoidal microthrombi were present predominantly in periportal areas. By 24 to 48 hours, liver cell edema and small focal necrotic lesions were prominent. After 48 hours, thrombi and hepatocellular necrosis were widespread. The animals succumbed to the infection within 5 days.

In C3H mice, during the acute phase of the infection granular flow and areas of focal necrosis were noted similar to the Balb/cJ mice. The acute phase was followed by persistent lesions and abnormal flow was seen adjacent to these focal areas of necrosis. By 2 months, a large number of granulomatous lesions were distributed throughout the liver parenchyma with concommitant distorted flow patterns.

These abnormalities were in sharp contrast to the normal flow studies in the resistant A/J mice despite the presence of virus as demonstrated by both immunofluorescence and recovery and growth of virus in all strains studied.

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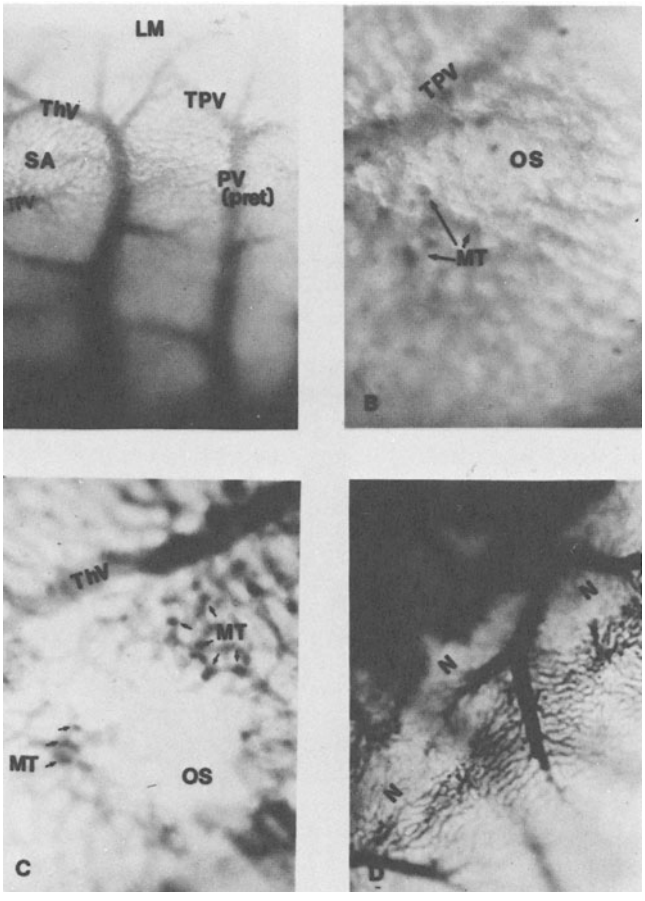

Figure 1

Studies of the In-Vivo Microcirculation in Balb/cJ mice:
(A) Normal microvascular pattern at liver margin (LM) x 60.
(B) Areas devoid of sinusoidal flow (OS) with microthrombi (MT) at the periphery of the lesion as seen 24 to 48 hours post infection x 200.
(C) Microthrombi and microcirculatory defect extend towards ThV, x 200.
(D) Confluent perivenular necrosis (N) x 125.
SA=Simple acinus TPV=Terminal portal venule ThV=Terminal hepatic venule PV (pret)= Preterminal branch of portal vein.

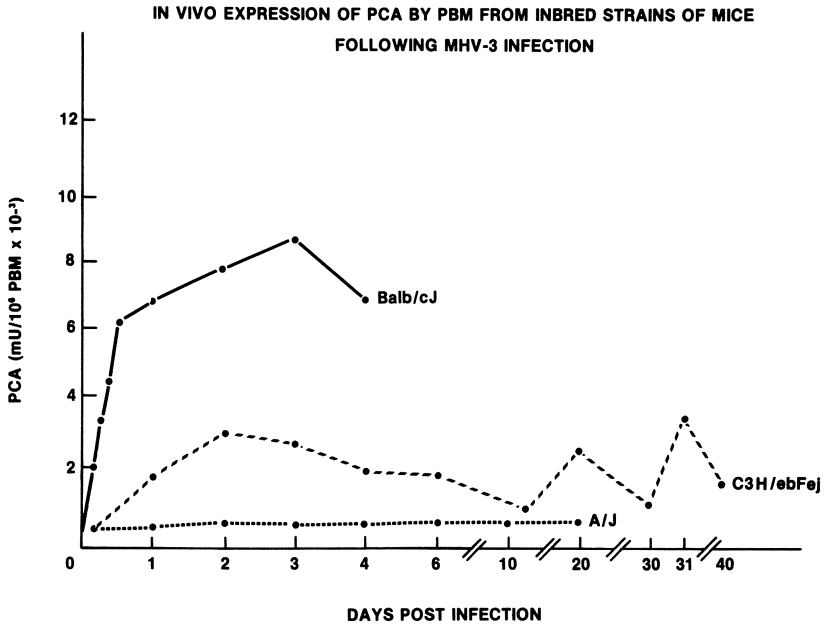

Figure 2

CONCLUSIONS

This study demonstrates:

1.Virus is present within the livers of resistant, semi-susceptible and susceptible mice.

2.Monocyte PCA is expressed within 4 hours following infection in susceptible animals. No PCA is expressed in resistant mice.

3.MHV-3 infection induces severe and progressive hepatic microcirculatory abnormalities in susceptible Balb/cJ mice and in the semi-resistant C3H mice. They consist of granular flow, microthrombi, liver cell edema and necrosis. No microcirculatory changes were noted in the fully resistant A/J mice.

We postulate that monocytes expressing surface PCA could initiate microcirculatory flow abnormalities with resultant microthrombi, endothelial cell injury and hepatocellular necrosis and are an important factor in the pathogenesis of tissue injury.