increase of blood flow was observed in the median lobe, while blood flow to the caudate lobe decreased. PT and antipyrine clearance decreased 7 and 14 days after transplantation. RES function was similar in all groups.

Conclusion. Partial liver transplantation with arterialization of the graft may be used for the study of liver regeneration in liver transplanted rats. Using microsurgical techniques, blood flow was readily restored in the graft. Growth in the volume of the transplant was evident, as early as 3 days after transplantation and continued 28 days after transplantation. RES function of the transplant was intact.

134 Hepatotrophic Effect of Cyclosporine A on Ischemic and Regenerating Liver

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Two years ago in Berlin we showed our results on the enhancing effect of CsA on hepatic regeneration following liver ischemia and hepatectomy. We have extended our experimental series in order to reach a better understanding of the hepatotrophic effects of CsA.

Material and Methods. Male Sprague-Dawley rats (250 g) have been used. 70% hepatectomy and/or i.p. inoculation of CsA (20 mg/kg the day before and 24 prior to operation) were performed in groups of 7 animals, either normoperfused or following 15 min of hepatic ischemia. Liver perfusion was interrupted by clamping the celiac trunk, the superior mesenteric artery and the hepatic pedicle. Animals were sacrificed 24 h after hepatectomy or liver ischemia, hepatocytic DNA content was measured by means of microspectrocytophotometry.

Results. Are presented in terms of the percentage of hepatocytes undergoing (%RH) and the ratio of mean values of DNA content in regenerating and 'static' hepatocytes (regenerative gradient: RG). (1) Controls: %RH = 1.21, RG = 2.15; (2) CsA: %RH = 4.01, RG = 2.38; (3) 70% hepatectomy: %RH = 22.29, RG = 1.60; (4) 70% hep. + CsA; %RH = 44.6, RG = 1.89; (5) ischemic Liver (I.L.): %HR = 0.75, RG = 2.16; (6) I.L. + CsA: %RH = 3.43, GR = 2.04; (7) I.L. + 70% hep.: %HR = 8.85, RG = 1.73; (8) I.L. + 70% hep. + CsA: %HR = 13.16, RG = 2.28.

Conclusions. (1) Liver ischemia has reduced the %RH in hepatectomized animals ($p<0.005$) but it has not modified the RG. (2) CsA has induced hepatocytic regeneration both in normoperfused and ischemic liver ($p<0.05$) and it has increased the %RH following 70% hepatectomy ($p<0.05$). (3) CsA has reduced the deleterious effect of warm ischemia but without reaching normal values. (4) CsA has increased the RG in all four experimental series ($p<0.05$).

135 Changes in Gene Expression during Liver Regeneration Surgically Induced: Effect of 4-Epi-Doxorubicin Pre-Treatment

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Liver regeneration is a highly regulated process which involves both positive and negative signals able to promote DNA replication and also to terminate the replicative wave.

Since two-thirds partial hepatectomy (PH) is also a well established experimental procedure to stimulate cellular growth in normally quiescent hepatocytes, we have adopted this technique in order to evaluate, at the molecular level, the mechanism by which the pharmacological compound 4-epi-doxorubicin affects this process. With this aim in view we treated 25 male Sprague-Dawley rats (162 ± 10 g) once a week for seven consecutive weeks with 4-epi-doxorubicin i.v. (1.25 mg/kg body weight; final vol. 5 ml/kg body weight). An equal number of animals, housed in a similar condition, were the normal controls. All rats underwent PH or sham hepatectomy between 8 and 11 a.m. and were sacrificed 0, 1, 2, 4, 8, 12, 18, 24, 36, 72 and 96 h after the operation. Total hepatic RNA were subjected to Northern blot hybridization with the following cDNA clones: c-fos, TGF β1, procollagen α1 (I) and albumin. The radiolabeled bands were quantified with scanning densitometry.

The Northern analysis showed that 4-epi-doxorubicin interferes with the liver regeneration by means of a lower and delayed expression of the considered genes. This was especially evident for the c-fos protooncogene, a marker of the prereplicative period. In fact, while with