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REGENERATIVE RESPONSE OF HEPATOCELLULAR TRANSPLANTS PLACED IN THE SPLEEN.

The functionalism of hepatocytes inoculated into the spleen has already been assessed. This work was designed to check the ability of these cells to response to regenerative stimuli.

MATERIAL and METHODS. Syngeneic female Fisher rats were used as receptors and donnors (200 g). Hepatocytes were isolated by continous perfussion with collagenase (0.5%) and the survival rate (94 +/- 2%) was assessed by means of the Tripan Blue exclusion test. 22 million of hepatocytes suspended in 1 cc of EMEN's solution were inoculated into the spleen. 70% hepatectomy was performed 24 h after inoculation. Daily doses of CsA (20 mg/kg i.p.) were administered from the day before transplantation. Four groups of seven animals have been considered: (I) Control, (II) 70% Hepatectomy, (III) CsA, (IV) 70% Hepatectomy + CsA. Animals were sacrificied 48 h. after inoculation, and hepatocytes' DNA content was measured by means of a microcytoespectrophotometric method. Mean percentage of regenerating hepatocytes (MPRH) was then assessed.

RESULTS. Hepatic MPRH was: (I) 7.3%, (II) 33.95%, (III) 20.79%, (IV) 29.77%. Splenic MPRH was: (I) 5.4%, (II) 37.44%, (III) 22.64%, (IV) 26.63%. Liver hepatocytes of animals with heterotopic implants showed a regenerative response similar to control livers: both 70% hepatectomy and CsA (alone or combined) increased MPRH ($p<0.05$), though the former induced the strongest response ($p<0.05$ vs CsA). There were not significant differences between MPRH of hepatic and splenic hepatocytes.

CONCLUSIONS. Inoculation of hepatocytes into the spleen induces a low regenerative response both in hepatic and splenic hepatocytes. Hepatocytes inoculated into spleen respond to regenerative stimuli (70% hepatectomy and CsA) similarly to hepatic hepatocytes.

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EXPERIMENTAL AND CLINICAL EVALUATION OF CAPSULAR AND PARENCHYMAL TOTAL LIVER PERFUSION

It is important, clinically, to be able to monitor liver blood flow because its metabolic functions are influenced by impairment of the hepatic circulation. However, this monitoring requires manipulation of the portal vein or hepatic artery and does not reflect total liver perfusion. On the other hand, it is not clear whether total hepatic blood flow can be more representatively estimated, on the liver surface or intraparenchymally. Therefore, the purpose of this study is the correlation of liver blood flow measurements obtained - by means of laser-Doppler flowmetry - from the liver surface and deep intraparenchymally, both in rats and humans.
In 23 Wistar rats and 10 biliary surgery patients, anaesthetized prior to gallbladder removal, liver microcirculation was measured first with a standard probe at 4 points of the capsular surface, and consequently at 4 points deep within the parenchyma, using a needle probe, the probes being connected to the Periflux PF2B [Perimed Sweden] laser-Doppler flowmeter. Signals were stored and analysed using Perisoft software [Perimed Sweden] in an IBM PS2. Our findings revealed that laser-Doppler measurements on the liver surface and within the parenchyma were well correlated, as no statistically significant differences were found either in rats or humans. Arterial blood pressure was monitored and remained constant during microcirculatory measurements.
It is concluded that laser-Doppler flowmetry for monitoring of total liver perfusion can be applied either on the capsular surface or within the hepatic parenchyma.

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ASSOCIATION OF MULTIPLE ENDOCRINE NEOPLASIA 2A AND CONGENITAL AGANGLIONIC MEGACOLON (HIRSCHSPRUNG's DISEASE)

Concurrence of Hirschsprung's disease in a family with Multiple Endocrine Neoplasia (MEN) 2A has been reported by Verdy et al (Gut 1982;1:603-607). We have identified a similar concurrence in two male siblings of a large North American kindred. The first sibling presented with chronic constipation and underwent resection at the age of 3 for typical Hirschsprung's with rectosigmoid aganglionosis. The child subsequently had a total thyroidectomy for unilateral medullary thyroid carcinoma at the age of 9. The diagnosis of congenital aganglionic megacolon was made in the second sibling shortly after birth. The presence of C-cell disease in this child, age 8 years, is suspected by a recent increase in the plasma concentration of calcitonin following pentagastrin stimulation. Neither child has evidence of hyperparathyroidism or pheochromocytoma. No clinical features of aganglionic megacolon are present in a female sibling or the mother, both affected with MEN 2A, or in unaffected family members. Other characteristics of the kindred include medullary thyroid carcinoma or C-cell hyperplasia in 54 individuals, hyperparathyroidism in 6 patients, and pheochromocytoma in 6 family members. As in MEN 2B, gastrointestinal symptoms may antedate the appearance of C-cell disease and identify children at risk for developing the MEN 2A syndrome. The possibility of Hirschsprung's disease should be considered in affected family members with MEN 2A and chronic constipation. The genetic mechanism responsible for this variation in the expression of the syndrome will be of interest.

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Flow Cytometric measurements of DNA-Content pH, cell volume and esterase activity in benign and malignant thyroid tissues

Cytological criteria of cell aspirations in thyroid tumors do often not allow a definitive diagnosis about the dignity of the tumor.It was the purpose of this study to measure the cellular DNA-content,esterase activity,intracellular pH and cell volume for better distinction of benign and malignant thyroid lesions.Method:193 thyroid specimens (thyroid carcinoma:25,follic.adenoma: 41,atoxic nodular goiter:92 and follicular adenoma after treatment with Carbimazol:35) were measured immediately after operation by means of flow cytometry.Results: In 76% of the thyroid carcinomas DNA-aneuploidy was demonstrated.In benign thyroid lesions, however,21%of the specimens revealed DNA-aneuploidy as well.Thus,the determination of the ploidy status in thyroid tumors as a single diagnostic parameter is of limited value.Furthermore significant differences between benign and malignant thyroid lesions could be determined in cell volume of epithelial and inflammatory cells ($p<0,001$), esterase concentration of epithelial and inflammatory cells ($p<0,01$) and intracellular pH ($p<0,05$).Hereby the sensitivity and specifity could be increased to 80% and 88% respectively.