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TRANSPLANTABILITY AND FURTHER PROGRESSION OF NEOPLASTIC NODULES INDUCED IN RAT LIVER BY AN INITIATION-PROMOTION-INITIATION PROTOCOL

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The neoplastic nature of secondary foci induced within islands of precancerous cells by an initiation-promotion-initiation protocol (Scherer et al., IARC Sci. Publ. 56, 57-66, 1984) has been investigated. Infusion of 20,000 to 100,000 viable focus cells into a mesentheric vein of isogenic rats led to multiple tumour foci - especially if focus cells were applied to partially hepatectomized rats. Ultrastructurally the transplanted tumour foci were characterized by increased cell size, abundance of mitochondria, distorted rough endoplasmic reticulum lacking parallel-arrayed stretches and by well developed smooth endoplasmic reticulum containing glycogen. Progression of transplanted neoplastic foci was studied after a promotion-initiation cycle consisting of a selection regimen (AAF) followed by a single dose of the direct acting carcinogen ENU. The observed (focal) progressive changes were into the direction of more pronounced ATPase and G6Pase deficiency combined with broadened trabeculae. Loss of glycogen storing capacity was generally related to an increase again of the enzyme-histochemical G6Pase activity. It is concluded that neoplastic foci are an intermediate stage in the evolution of hepatocellular carcinoma of the rat.

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SKIN TESTING WITH TETANUS TOXOID FLUID VACCINEAN TO ASSESS CELLULAR IMMUNITY

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Skin testing with recall antigens is a safe and easy method to assess cellular immunity and for diagnosis of disorders in T-cell function.

A suitable antigen for skin testing appears to be tetanus toxoid, prepared as fluid vaccine. We carried out such a test in healthy children before and after regular vaccination with DPT or DT vaccine and in vaccinated children under cytostatic treatment of malignant diseases. Children before vaccination showed no local reaction. After DPT-vaccination we observed positive skin reactions in all children. However the skin reactions were different and dependent on the intensity and duration of immunosuppressive therapy. Side reactions did not occur. The total number of lymphocytes and also the number of sheep erythrocyte binding cells remained constant. The results of lymphocyte transformation tests and leucocyte adherence tests corresponded well.

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EFFECTS OF PHENOBARBITAL AND HYPOLIPIDEMIC DRUGS ON PHENOTYPIC APPEARANCE OF PUTATIVE CANCER PRESTAGES IN RAT LIVER

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Various liver tumour promoters represented by phenobarbital (PB) accelerate growth of putative preneoplastic foci in rat liver as identified by presence of γ-glutamyltransferase (γ-GT), eosinophilia, etc. (foci type I). Furthermore, these agents induce the expression of adaptative increases in drug metabolism and growth in foci as well as in normal liver. The relevance of these increases for tumour promotion has now been investigated in dose-response studies with PB and 3 different isomers of hexachlorocyclohexane (HCH) in foci and normal liver. Another class of liver tumour promoters is represented by hypolipidemic drugs such as nafenopin or clofibrate. These agents differ from PB by their effects on normal liver and on putative preneoplastic foci. While type I foci tend to disappear during nafenopin treatment, foci with different morphological and histochemical properties show up (foci type II). These lesions may express another gene programme that provides a growth advantage during treatment with hypolipidemic drugs.
