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Liver lectins: mediators for metastases?

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Summary. Development of liver metastases in 1542 cancer patients was investigated. It was found that in certain liver diseases the incidence of liver metastases was reduced compared to that in cancer patients with otherwise normal livers. We propose that this reduction may be due to a reduced function of the liver-specific lectins.

In certain liver diseases there is a marked increase of serum asialoglycoproteins[1]. This phenomenon may arise from an alteration of the liver cell plasma membrane, whose surface lectins recognize and eliminate asialoglycoproteins. This mechanism, which has been reviewed recently[2], has been investigated for various glycoproteins in our laboratory[3].

It has been claimed by Springer et al.[4] and Uhlenbruck et al.[5,6] that asialoglycoproteins of the tumor cell surface may carry tumor cell-characteristic carbohydrate groups, for instance the Thomsen-Friedenreich receptor[7], and it has been further postulated that these structures could also be responsible for the arrest of metastasizing tumor cells[7].

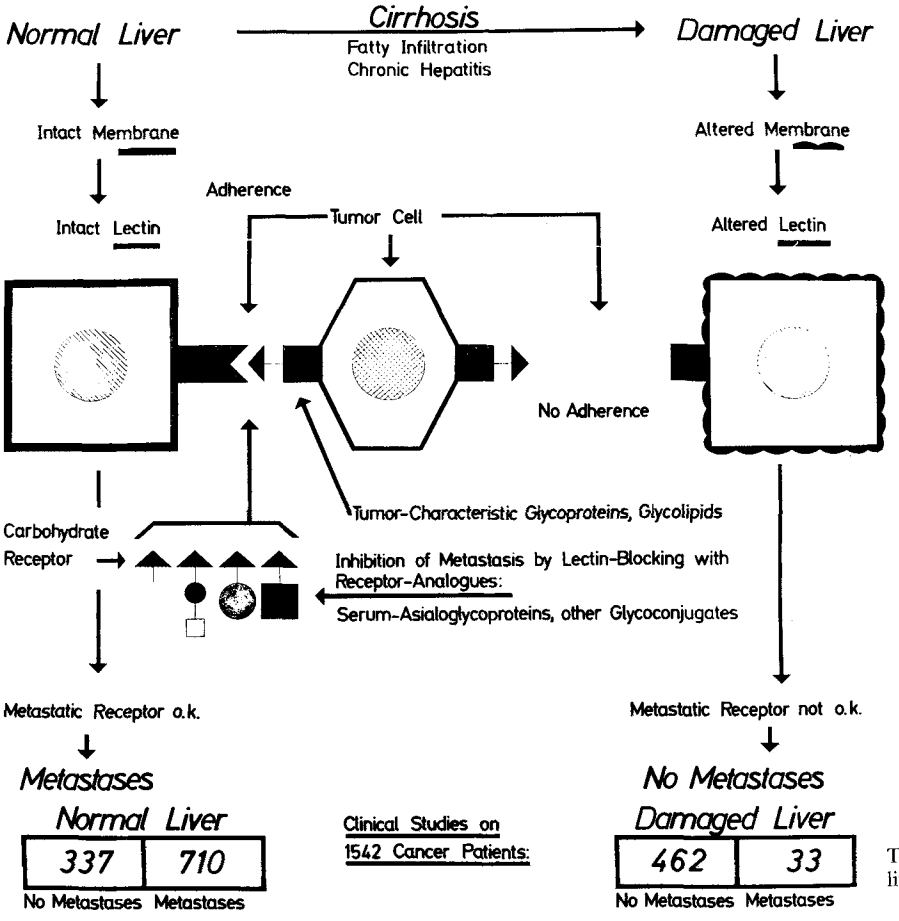

Table: Relationship between liver diseases and liver metastases.

Because the liver contains lectins and these lectins seem to be diminished in their function in cases of chronic liver cell diseases[8], we decided to examine the correlation between liver disease and liver metastasis. According to the theory discussed above it could be predicted that the adherence of tumor cells in diseased livers should be diminished, and in patients with liver diseases like cirrhosis, fatty infiltration, and chronic hepatitis the occurrence of liver metastases would be the exception. However, dysfunction of the galactose-binding protein is only one of the pathologies in liver disease that might effect metastasis to this organ. Therefore, one should only consider this clinical study as the basis for a hypothesis to be tested experimentally.

We investigated the case history and pathology of 1542 unmatched deceased cancer patients and found that in patients with the above-mentioned liver diseases, as well as with cancer, which usually tends to metastasize into the liver, the number of metastases observed in the liver was indeed reduced. Our results are schematically summarized in the table. These data lend support to the idea that organ-characteristic lectins may play an important role in the organ-specific distribution of metastases. Experiments in animals already support this suggestion for certain tumors[9,10].

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Long term effects of neonatal hypothyroidism on pituitary estradiol binding sites in the female rat

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Summary. Two months after recovery from a perinatal hypothyroidism (PTU), the total amount of pituitary estradiol binding sites (EBS) was still dramatically reduced, but the actual concentration of EBS had returned to control levels.

There is general agreement that hypothyroidism leads to impaired gonadotropin secretion[1,2], prolonged estrus[3], and increased estrogen retention in the uterus[4]. At the cellular level, thyroid hormones were shown to modulate uterine responses to estrogen[5,6], and significant alterations in the pituitary concentrations of estradiol binding sites (EBS) were shown to occur in thyroidectomized adult rats[7] and in thyroid hormone deprived neonates[8].

Since thyroid hormone deficiency in the perinatal period clearly induces irreversible cellular and functional abnormalities in the development of the central nervous system[9,10], the question arises whether the disruptive effects of hypothyroidism on the reproductive system may be ascribed at least partially, to a persistent lack of pituitary EBS. The present study was designed to answer this question.

Material and methods. 10 pregnant Wistar rats (IFFA CREDO, Lyon) were housed in a temperature-controlled room (21 ± 1 °C) under natural lighting, with free access to water and standard chow (Provimi, Paris). Male pups were removed at birth, while the females were divided randomly into nursing families of 8 rats each. Control neonates were weaned after 3 weeks, in contrast to 5 weeks for their hypothyroid congeners. Hypothyroid offspring were obtained from dams by a daily gastric intubation with 50 mg of

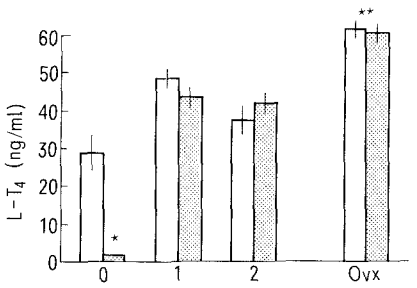

Figure 1. Plasma thyroxine levels in normal (open bars) and neonatal PTU-induced hypothyroid animals (hatched bars) at the end of the 5-week PTU treatment (0), 1 (1) and 2 (2) months after PTU withdrawal, and 1 week after ovariectomy (Ovx). * $p < 0.01$ vs age-matched controls; ** $p < 0.01$ vs intact animals of both groups.

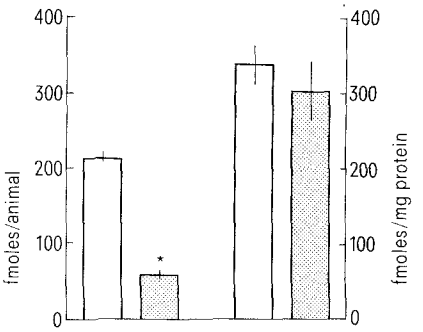

Figure 2. Pituitary estradiol binding sites concentrations in normal (open bars) and neonatal hypothyroid animals (hatched bars), 2 months after PTU withdrawal. Rats were ovariectomized 1 week before binding sites measurement. * $p < 0.01$ vs control rats.