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].

1 Marshall, J.S., Green, A.M., Pensky, Z., Williams, S., Zinn, A., and Carlson, D.M., J. clin. Invest. *54* (1974) 555.
2 Ashwell, G., and Harford, J., A. Rev. Biochem. *51* (1982) 531.
3 Newman, R.A., Fricke, U., Klein, P.J., Uhlenbruck, G., and DeVries, A.L., J. clin. Chem. clin. Biochem. *18* (1980) 31.
4 Springer, G.F., Desai, P.R., and Scanlon, E.F., Cancer *37* (1976) 169.
5 Uhlenbruck, G., and Gielen, W., Fortschr. Neurol. Psychiatr. *38* (1970) 202.
6 Newman, R.A., Klein, P.J., Uhlenbruck, G., Citoler, P., and Karduck, D., J. Cancer Res. clin. Oncol. *93* (1979) 181.
7 Uhlenbruck, G., Immun. Commun. *10* (1981) 251.
8 McFarlane, I.G., Clin. Sci. *64* (1983) 127.
9 Schirrmacher, V., Cheingsong-Popov, R., and Arnheiter, H., J. exp. Med. *151* (1980) 984.
10 Schirrmacher, V., personal communication.

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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

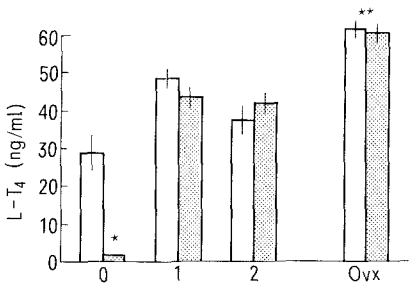

Figure 1. Plasma thyroxine levels in normal (open bars) and neonatal PTU-induced hypothyroid animals (hatched bars) at the end of the 5-week PTU treatment (0), 1 (1) and 2 (2) months after PTU withdrawal, and 1 week after ovariectomy (Ovx). * $p < 0.01$ vs age-matched controls; ** $p < 0.01$ vs intact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

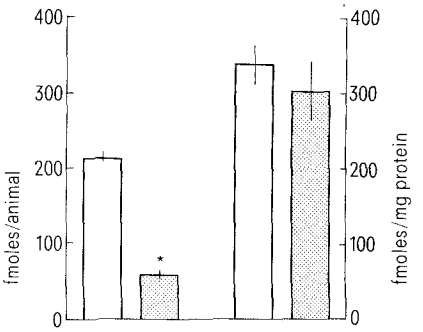

Figure 2. Pituitary estradiol binding sites concentrations in normal (open bars) and neonatal hypothyroid animals (hatched bars), 2 months after PTU withdrawal. Rats were ovariectomized 1 week before binding sites measurement. * $p < 0.01$ vs control rats.

propylthiouracil (PTU) from the 18th day of gestation until weaning. The pups were weighed at regular intervals, and blood samples were collected by cardiac puncture under Nembutal anesthesia, 1 and 2 months after cessation of the anti-thyroid treatment, and the plasma samples were stored at −30 °C until hormonal measurements. Simultaneously with the 2nd blood sampling, the animals were ovariectomized in order to avoid interference with endogenous estrogens. 1 week later, the rats were killed by decapitation, blood was collected from the trunks, and pituitaries were quickly removed, blotted free of blood and chilled in ice-cold TEM buffer (10 mM tris, HCl, pH 7.4; 1.5 mM EDTA; 12 mM monothioglycerol).

The pituitary estradiol binding sites were measured at 2 °C by the protamine precipitation method described earlier[8,11]. Protein concentrations in the replicates were determined spectrophotometrically[12], and plasma thyroxine (L-T_4) concentrations were measured by radiocompetition against human thyroxine-binding-globulin[8].

One-way ANOVA according to BMDP statistical software was performed to detect significant differences between control and hypothyroid groups.

Results and discussion. Although neonatal hypothyroidism caused a marked and persistent delay in body growth, body weights started to increase two weeks after the cessation of the anti-thyroid treatment. The body weight increment then followed a similar pattern in hypothyroid and control animals from the age of 9–10 weeks on, which agrees with previous reports[13]. Similarly, plasma L-T_4 levels, which were previously shown to be nearly undetectable throughout the anti-thyroid treatment[8], had already returned to normal levels 1 month after the PTU withdrawal (fig. 1). At this stage they did not differ from L-T_4 titers in 13-week-old animals, a result in keeping with restoration experiments in adult rats[14]. Moreover, the subsequent ovariectomy led to a 40% rise ($p < 0.01$) of plasma L-T_4 levels in both controls and initially hypothyroid animals, suggesting that PTU-induced neonatal hypothyroidism had no apparent after-effects on ovary-thyroid interactions.

On the other hand, 2 months after cessation of the PTU treatment, the initially hypothyroid group still displayed a 75% reduction in the total amount of available EBS in the pituitary (fig. 2). It may tentatively be assumed that this lowered amount in pituitary EBS may, indeed, be part of the mechanism whereby neonatal hypothyroidism leads to persistent dysfunctions of the reproductive system. However, considering the actual concentrations in pituitary EBS as expressed in fmoles/mg protein, the 2 groups of rats were indistinguishable. Clearly, the long-lasting lack of pituitary EBS in rats suffering from perinatal hypothyroidism may be attributable to an impaired pituitary growth, rather than to decreased cellular synthesis of EBS. Consequently, the specific decrease of pituitary estradiol binding sites previously observed in hypothyroid rats during the early neonatal period[8] appears essentially as a transient and reversible postnatal effect.

1 Bruni, J.F., Marshall, S., Dibbet, J.H., and Meites, J., Endocrinology *97* (1975) 558.
2 Freeman, M.E., La Rochelle, Jr, F.T., and Moore, R.B., Endocrinology *99* (1976) 713.
3 Gilman, J., and Gilbert, C., J. Obstet. Gynec. Br. Commonw. *60* (1953) 445.
4 Ruh, M.F., Ruh, T.S., and Klitgaard, H.M., Proc. Soc. exp. Biol. Med. *134* (1970) 558.
5 Gardner, R.M., Kirkland, J.L., Ireland, J.S., and Stancel, G.M., Endocrinology *103* (1978) 1164.
6 Steinsapir, J., Rojas, A.M., Mena, M., and Tchernitchin, A.N., Endocrinology *110* (1978) 1773.
7 Cidlowski, J.A., and Muldoon, T.G., Endocrinology *97* (1975) 59.
8 Barbanel, G., and Assenmacher, I., Molec. cell. Endocr. *28* (1982) 247.
9 Ford, D.H., and Cramer, E.B., in: Thyroid hormones and brain development, p. 1. Ed. G.D. Grave. Raven Press, New York 1977.
10 Dussault, J.H., and Fisher, D.H., in: Clinical Neuroendocrinology, a pathophysiological approach, p. 225. Eds G. Tollis et al. Raven Press, New York 1977.
11 Barbanel, G., and Assenmacher, I., Molec. cell. Endocr. *18* (1980) 227.
12 Kalb, V.F., and Bernlohr, R.W., Analyt. Biochem. *82* (1977) 362.
13 Kikuyama, S., Nagasawa, H., Yanai, R., and Yamanouchi, K., J. Endocr. *62* (1974) 213.
14 Burstein, P.J., Draznin, B., Johnson, C.J., and Schalch, D.S., Endocrinology *104* (1979) 1107.

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Corticoadrenal and behavioral response to open field in pairs of male rats either familiar or non-familiar to each other

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Summary. The effect of the presence either of a familiar or non-familiar conspecific animal on serum corticosterone and some behavioral responses in the open field was studied in male Sprague-Dawley rats. Animals tested in presence of a familiar animal showed a higher corticosterone response and a higher defecation rate. It suggests that rats experienced more emotional reactivity in presence of a familiar animal than in presence of a non-familiar one. Time spent in social interaction was higher in non-familiar pairs; however, ambulation and rearing were lower, suggesting competition between social investigation and novel environment exploration.

Using various behavioral measures of fear, many investigators have noted that fear experienced by rats in a stressful situation was reduced by presence of a conspecific animal[1–3]. However, contradictory results have been reported following work dealing with the effect of conspecifics on corticoadrenal response to stress[4–6]. This apparent lack of relationship between behavioral responses and corticoadrenal activity is not surprising since no correlation has been observed between defecation (the most often used index of fear in the rat) and serum corticosterone in response to