differs significantly ($p = 0.01$) from the expected 56% mortality. *N. tasmanicus* was observed to defecate 6–20 small drops of excreta per day. This habit, plus the finding that P.I.B. remain highly infective in the feces of *N. tasmanicus*, suggests that the predators may be important as virus disseminators in the field.

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The adequacy of thiamine in liquid diets used in animal models of alcoholism

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Summary. The effects of chronic administration of 2 types of liquid diets on brain thiamine pyrophosphate (TPP) levels have been investigated. With the Lieber-DeCarli diet, rats in the control group had significantly lower TPP levels compared with those of the ethanol group. The Nutrament diet used in mice was apparently adequate in the thiamine supply.

The development of credible animal models of alcohol intake for the study of the mechanisms of tolerance and physical dependence has occurred only within the last 10–15 years[2,3]. One of these involves the administration of a liquid diet in which ethanol provides as much as 30–40% of the calories[4–7]. Although the liquid diets are generally considered nutritionally adequate, it has not been definitively established that they necessarily contain adequate levels of all nutrients or that these are fully available for utilization at the subcellular level[8].

Conflicting evidence exists in animal studies as to whether the longterm administration of alcohol alters thiamine and thiamine pyrophosphate levels in tissues. Kiessling and Tilander[9] reported that rats which were forced to drink an aqueous solution of ethanol for 7 months had significantly lower thiamine and thiamine pyrophosphate levels in the liver compared to controls given water and sucrose solution. However, other investigators have reported no changes in tissue levels of TPP in rats exposed chronically to dietary alcohol[10,11].

Methods. Male Wistar rats (23–25 days old) and C57BL/6J mice (63–70 days old) were purchased from Woodlyn Laboratories Ltd., Guelph, Ontario, Canada and the Jackson Laboratories, Bar Harbor, ME, respectively. Rats were divided into 4 groups, with $N = 10$ in each: group A received the Lieber-DeCarli ethanol liquid diet (Bio-Serv Co., Inc., Little Silver, N.J.) ad libitum as the sole source of food and water; group B was pair-fed the isocaloric control diet (carbohydrate substituted for ethanol); group C was pair-fed the same diet as group A except that an equal volume of water was substituted for ethanol; group D received Teklad pellets and water ad libitum. The diets were administered for 6 weeks. In another experiment, mice were divided into 4 groups: group A received ad libitum a chocolate flavored Nutrament diet (Mead Johnson Nutritionals) containing 6% (v/v) ethanol[4]. The same diet, except that an isocaloric sucrose solution or an equal volume of water was substituted for ethanol, was pair-fed to groups B and C respectively. The diets were administered for 11 days. Another group of mice (group D) was fed ordinary food pellets and water.

Rats were sacrificed by decapitation and the heads were immediately dropped into liquid N_2 remaining there for at least 2 min. Mice were sacrificed by dropping them into liquid N_2. Procedures for sampling the cerebellum and for preparing perchloric acid extracts were the same as those previously described[12,13]. TPP was measured by the enzymatic-fluorometric method of Seltzer and McDougal[14].

Results and discussion. It is seen from Table 1 that rats fed the Lieber-DeCarli ethanol diet (group A) for 6 weeks did not have significantly lower TPP content in the cerebellum compared to those fed ordinary food pellets and water (group D), or the liquid diet with water substituting for ethanol (group C). However, significantly lower TPP levels were found in rats fed the isocaloric control diet (group B). The decrease in TPP in this group could be the result of an

Table 1. TPP contents in rat cerebellum after chronic administration of Lieber-DeCarli liquid diet

Diet	TPP (μmoles/kg wet wt)*
Ethanol (group A)	10.38 ± 0.99
Isocaloric control (group B)	8.11 ± 0.83**
Water control (group C)	11.03 ± 0.49
Ordinary food pellets and water (group D)	11.04 ± 0.66

* Mean values ± SD; $N = 10$. ** Significantly different from groups A, C and D; $p < 0.001$.

Table 2. TPP contents in mouse cerebellum after chronic administration of Nutrament liquid diet

Diet	TPP (μmoles/kg wet wt)*
Ethanol (group A)	14.06 ± 2.52
Isocaloric control (group B)	14.65 ± 2.39
Water control (group C)	14.32 ± 2.05
Ordinary food pellets and water (group D)	13.31 ± 1.08

* Mean values ± SD; $N = 8$.

increased utilization of thiamine due to the higher carbohydrate content in the diet. It is known that carbohydrates tend to increase thiamine consumption and enhance the development of neurologic dysfunction in thiamine-depleted animals[15].

Mice that were fed the different forms of Nutrament diet (groups A, B, and C) for 11 days had more or less the same TPP contents in the cerebellum (table 2) and the values were not significantly different from those seen in mice that were fed ordinary food pellets and water (group D).

We estimated from the amount of diet consumed, mean body weights and thiamine content of the diet, that the daily intake of thiamine by rats fed the Lieber-DeCarli diet was 180–210 µg/kg b.wt. Since the daily requirement of thiamine for rats is 1.25 mg/kg food[16], it can be estimated that the minimal daily thiamine intake for rats is 110–190 µg/kg b.wt. Therefore the rats that were fed the Lieber-DeCarli diet had a daily thiamine intake just above the recommended daily requirement. In the case of Nutrament diet for mice, we estimate the daily thiamine intake from the diet to be 1400–2000 µg/kg b.wt. This is about 3 times in excess of the estimated recommended minimal daily intake[16], namely, 480–600 µg/kg b.wt.

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Effect of praseodymium on drug metabolism in rat liver smooth and rough endoplasmic reticulum

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Summary. A small i.v. dose (3 mg/kg) of a light lanthanon, praseodymium, impairs the drug metabolizing capacity of both the smooth and rough fractions of rat liver endoplasmic reticulum. This decrease in the activity of drug metabolizing enzymes and in the amount of cytochromes P-450 and b_5 is more pronounced in the rough endoplasmic reticulum fraction.

Lanthanons include 15 elements (at. No. 57–71) which are very similar in their chemical and physical character. According to their biological effects these elements can, however, be divided into light (at. No. 57–62) and heavy (at. No. 63–71) lanthanons. The light lanthanons, including praseodymium (Pr) (at. No. 59), are highly hepatotoxic agents[1]. When administered i.v. they cause changes in the ultrastructure of liver cells and several investigations show that the primary attack of lanthanons occurs on the endoplasmic reticulum[2]. Electron microscopic pictures show that after i.v. administration of relatively small amounts of light lanthanons the rough endoplasmic reticulum (RER) decreases while the smooth, vesicular type of endoplasmic reticulum (SER) increases.

In the present study the effect of the light lanthanon, Pr, on the drug metabolism mainly associated with SER, has been compared in these two subcellular fractions of rat liver.

Materials and methods. Adult female Wistar rats (160–180 g) were used. They were given a standard diet (Altromin®) and tap water ad libitum, but 24 h before killing the food was withdrawn. Praseodymium was administered i.v. as a nitrate salt, $Pr(NO_3)_3$. 5 H_2O, in 0.9% saline solution corresponding 3 mg cation/kg. The animals were killed after 1 or 2 days, livers removed and homogenized in 0.1 M phosphate buffer, pH 7.4. To separate the SER and RER subfractions the supernatants obtained after 12,000 × g were submitted to a discontinuous gradient centrifugation according to Fleischer and Kervina[3]. The purity of these fractions was checked by electron microscopy.

To test the drug metabolizing capacity of these fractions the activity of aryl hydrocarbon hydroxylase (AHH) was measured according to Kuntzman et al.[4] and that of aniline hydroxylase (AH) as described by Kato and Gillette[5]. The cytochromes P-450 and b_5 were determined according to Omura and Sato[6] and protein was estimated by the method of Lowry[7].

Results and discussion. In accordance with our earlier findings[8] the administration of a light lanthanon decreases

Table 1. Effect of Praseodymium (3 mg/kg i.v.) on the activities of aryl hydrocarbon hydroxylase (AHH) and aniline hydroxylase (AH) in rat liver smooth (SER) and rough (RER) endoplasmic reticulum and whole microsomes 48 h after injection

	AHH activity (relative fluorescence units/mg protein)	Activity (%)	AH activity (µg p-aminophenol/mg protein/20 min)	Activity (%)
Microsomes (control)	2533 ± 66*	100.0	0.331 ± 0.054	100.0
Microsomes (Pr 3 mg/kg)	729 ± 226	28.8	0.169 ± 0.047	51.1
SER (control)	2450 ± 166	100.0	0.277 ± 0.033	100.0
SER (Pr 3 mg/kg)	720 ± 106	29.4	0.195 ± 0.037	70.4
RER (control)	2569 ± 24	100.0	1.506 ± 0.115	100.0
RER (Pr 3 mg/kg)	344 ± 166	13.4	0.722 ± 0.317	47.9

* ± SD.