The rate constants k_i of TSH secretion can be considered as measure of pituitary thyrotropic responsiveness to TRH normalized for triiodothyronine and thyroxine. The responsiveness is highest in euthyroidism, reduced in primary hypothyroidism, and lowest in hyperthyroidism. These differences indicate that the responsiveness to TRH is not only a function of feedback inhibition by triiodothyronine and thyroxine, but also a function of hitherto unknown factors. Neurogenic amines and polypeptides of hypothalamic origin are to be considered as possible candidates.

Equation 7 can be applied to predict the time course of TSH concentration in plasma of individuals after TRH stimulation, especially values at time t other than $t = 0$ and $t = 20$ min. Examples, one out of each group, are shown in the figure. The congruency of the measured data with the calculated points is fairly good, thus supporting the validity of the assumptions taken into account.

The effects of continuous chloroform and halothane anesthesia on plasma prolactin levels in ovariectomized estrogen-treated rats[1]

Marappa G. Subramanian and R. R. Gala[2]

Department of Physiology, Wayne State University School of Medicine, 540 E. Canfield, Detroit (Michigan 48201, USA),
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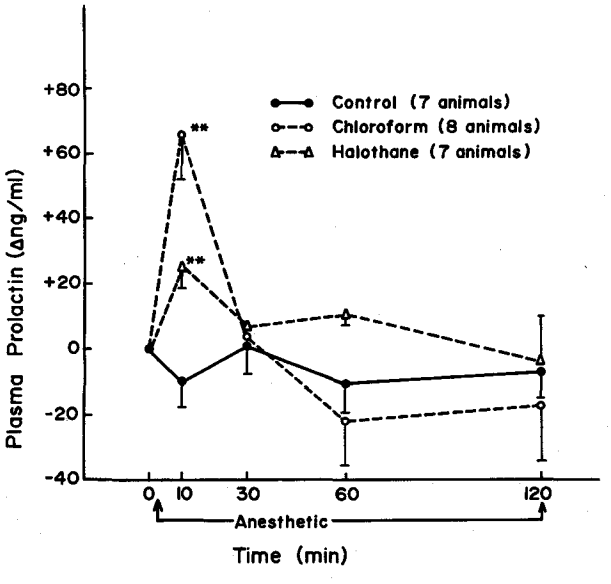
Summary. In ovariectomized, estrogen-treated rats bearing indwelling aortic catheters, continuous inhalation of chloroform or halothane resulted in increases in plasma prolactin levels 10 min after the exposure to the anesthetics. The plasma prolactin levels over the subsequent 2 h, however, were not significantly different from that of the control animals.

Previous studies from our laboratory examined the influence of injectable and inhalation anesthetics on prolactin release[3–5]. Ether increased plasma prolactin levels in both ovariectomized and ovariectomized, estrogen-treated rats[3–5] whereas methoxyflurane (MF) increased plasma prolactin only in estrogen-treated rats[5]. The present study was performed to determine the effects of 2 additional inhalation anesthetics, chloroform and halothane, on plasma prolactin levels in ovariectomized, estrogen-treated rats.

Materials and methods. Mature female Sprague-Dawley rats weighing 225–250 g were ovariectomized and housed in a room with controlled temperature (23 ± 2 °C) and lighting (14 h light, 10 h darkness, lights on at 06.00 h). 2–3 weeks later, a catheter was inserted into the left carotid as described in detail elsewhere[3]. At the time of catherization 0.5 mg of polyestradiol phosphate (1 mg Estradurin®, Ayerst Laboratories) was administered s.c. to each rat. The withdrawal of blood samples began 1 week after catheterization. The experimental procedure was as follows: on the day of sampling between 08.00 and 09.00 h an extension was attached to the indwelling catheter and the animals were left undisturbed for at least 60 min. After this equilibration period, a control sample (0.6 ml) was withdrawn (time 0). After each blood sample was obtained, the volume was replaced with an equal volume of saline warmed to 37 °C. In the control group subsequent blood samples were obtained at 10, 30, 60 and 120 min. In the experimental groups, after the 0 min sample, the animals were anesthetized in a large jar saturated with either chloroform or halothane (Fluothane®, Ayerst Laboratories) vapor and maintained under continuous anesthesia using a nose cone for the duration of the experiment (120 min). Additional blood samples were obtained 10, 30, 60 and 120 min after the initiation of anesthesia. The blood samples were immediately diluted with an equal volume of chilled phosphate buffer saline (pH 7.6) and centrifuged at 3 °C. The plasma obtained was stored frozen at −20 °C. Plasma prolactin levels were assayed by the double antibody radioimmunoassay[6] at 2 dilutions each in duplicate. Rat prolactin NIAMDD-RP-1, with a potency of 11 IU/mg, was the standard. Plasma prolactin values are expressed as ng/ml



The influence of continuous chloroform and halothane anesthesia on plasma prolactin levels in ovariectomized, polyestradiol phosphate-injected rats. Plasma prolactin levels are expressed as ng/ml change from the initial levels. Values represent the mean ± SEM at each point. Statistical comparisons were made between the control and experimental groups at the same time periods. ** $p < 0.01$.

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change from the 0 min values. Student's t-test[7] was used to assess the statistical significance between the control and experimental groups at each time period.

Results. 10 min after anesthesia, the plasma prolactin levels in the chloroform and halothane anesthetized groups were significantly higher ($p < 0.01$) than the unanesthetized control groups (figure). In the subsequent time periods the prolactin levels were not significantly different from that of the control group. With both chloroform and halothane, anesthesia was induced within 1–2 min after exposure to the anesthetic.

Discussion. The pattern of plasma prolactin response induced by chloroform and halothane in ovariectomized, estrogen-treated rats was similar, although the magnitude of rise and sharpness of decline was more pronounced with chloroform than with halothane. Such an acute rise and fall in the plasma prolactin levels was observed by us for 2 other inhalation anesthetics, ether and MF[4,5]. From the similarity of the responses observed, it is possible that all 4 inhalation anesthetics may act through a common neuroendocrine mechanism in releasing prolactin. Although Krulich[8] has reported that a central serotonergic mechanism is involved in ether-induced prolactin release in rats, recent reports[5,9] from our laboratory indicated the possible involvement of other biogenic amine systems as well.

In our experience, all 4 inhalation anesthetics release prolactin in estrogenized female rats, however, MF seems to be safer, easier to manage, and causes minimum respiratory difficulties.

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Nicotinamide and streptozotocin diabetes in the rat. Factors influencing the effectiveness of the protection

P. Masiello and E. Bergamini

Istituto di Patologia Generale dell'Università di Pisa, Via Roma 55, I-56100 Pisa (Italy), 10 August 1976

Summary. The effectiveness of nicotinamide in protecting against streptozotocin diabetes does not only depend on streptozotocin dosage but also on the age of the rats. Also, the extent of the protection suddenly decreases when the interval between streptozotocin and nicotinamide injections exceeds 1 h.

Many drugs can protect against the diabetogenic effect of alloxan but only nicotinamide is effective in the case of streptozotocin (SZ)[1]. It is known that this long-lived precursor of nicotinamide-adenine dinucleotides[2] prevents the destruction of NAD[3] and the subsequent decrease of the NAD levels in beta cells after SZ[4]. Also, pyridine nucleotides may be involved in insulin release induced by glucose[5,6]. The specificity of this interaction invited further research. It was found that protection depends on the dosage of both drugs[7,8] and that nicotinamide can even reverse the effects of SZ[7,9,10], although its efficacy decreases with the time elapsed after SZ administration[10]. However, quantitative information is still lacking which could explain the early damage of the beta cells and lead to a more accurate timing of the onset of no-return changes in this endocrine tissue.

In our first experiment, we administered nicotinamide (70, 140, 210 and 240 mg/kg b.wt, i.p.) 15 min before the i.v. injection of 50, 60, 70 or 80 mg/kg b.wt SZ to 130 g rats and we evaluated plasma glucose levels by a glucose-oxidase/peroxidase method (Glucosio-Test, Sclavo I.S.V.T., Siena) 24 h later. Results indicated that nicotinamide could let us detect differences among the effects of the slightly different doses of SZ, in spite of the similar

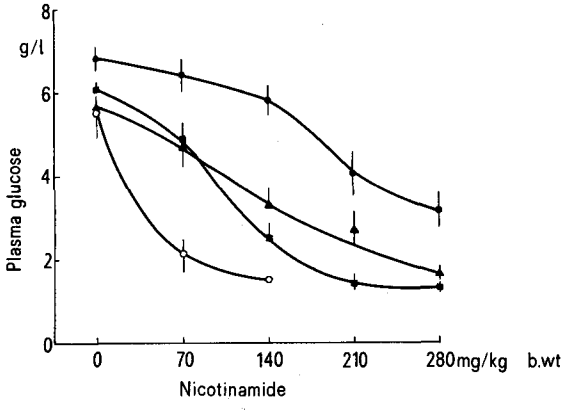

Fig. 1. Plasma glucose concentrations in 130 g male Wistar albino rats 1 day after the injection of different doses of streptozotocin (○, 50 mg/kg; ■, 60 mg/kg; ▲, 70 mg/kg; ●, 80 mg/kg b.wt) which followed the i. p. administration of the amounts of nicotinamide indicated on the abscissa. The interval between the 2 injections was 15 min. Means of 6 cases are given. Vertical bars represent 1 or 2 × SEM.

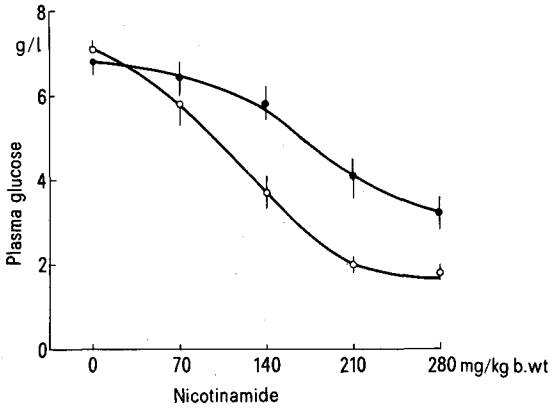

Fig. 2. Plasma glucose concentrations in 70 g (○) or 130 g (●) male Wistar albino rats 1 day after the i.v. injection of 80 mg/kg b.wt streptozotocin and nicotinamide (see figure 1). Means of 6 cases are given. Vertical bars represent 1 or 2 × SEM.