

Blood A levels attained during the hormone infusion in the 1st and 2nd series did not differ significantly ( $p > 0.05$ ). The concentration of A at the end of infusion was  $1.65 \pm 0.28 \mu\text{g/l}$  (1st series) and  $1.56 \pm 0.29 \mu\text{g/l}$  (2nd series).

**Discussion.** The results obtained show that the hyperglycemic effect of A is much smaller in the dogs previously exercising until exhaustion than in the same dogs infused at rest without preceding physical effort. This phenomenon cannot be attributed to the increased uptake of glucose by the muscles depleted of glycogen, since there was no significant increase in the muscle glycogen content following A infusion. The weaker effect of adrenaline after exercise may be caused by an exhaustion of the liver glycogen, insufficient gluconeogenesis, or by a decreased reactivity of the liver enzymatic systems to adrenaline. A decrease of the liver glycogen content after exhausting physical work has been found in human subjects; however some amount of the liver glycogen seemed to be not available for glycogenolytic factors acting during exercise<sup>8</sup>. In the present investigation, FFA response to A

in the dogs infused under resting conditions did not differ significantly from that found after exhausting exercise. On the contrary, an increased adipose tissue responsiveness to NA after preceding physical activity was described in humans<sup>9</sup>. Adrenaline-induced increase of LA after exercise in spite of glycogen depletion from the working muscles suggests that it originated from non-working muscles.

Summarizing, the data obtained in the present study demonstrate that the hyperglycemic effect of A is markedly reduced after prolonged exercise. However, it is still possible to increase blood glucose concentration by adrenaline in this situation. Thus, a decrease in blood A level may be partly responsible for the hypoglycemia found at the end of prolonged exhausting exercise in dogs.

**Résumé.** Les changements de concentration de glucose, FFA et LA résultant d'une infusion intravéneuse d'adrénaline ont été étudiés chez des chiens ayant été soumis à un exercice physique prolongé. On a constaté un abaissement de l'effet hyperglycémique de l'adrénaline. Les autres paramètres changeaient semblablement, comme dans les conditions de contrôle, sans effort physique préalable.

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## Catecholamines in Fetal and Neonatal Rabbit Heart

It is well known that important physiological changes occur at birth<sup>1</sup>. The fetal suffering conditions which exist at parturition, and the sudden adaptation of the newborn to atmospheric life, are probably accompanied by modifications of neuro-endocrine system activity. The adrenal catecholamines store has been found to decline immediately after birth, in rats<sup>2</sup> and rabbits<sup>2,3</sup>, while in rabbits the level of plasma norepinephrine increased at parturition<sup>4</sup>. This study was undertaken to determine whether or not the cardiac catecholamine store changes in the fetus near term and within the first few hours after parturition.

**Materials and methods.** The experiments were carried out on fetuses and new-born rabbits of the white New Zealand strain. In the last 2 days of pregnancy (term = 31 days), the female rabbits were killed by air embolism, laparotomy was performed and the fetuses were taken out immediately and decapitated. The hearts were quickly removed, washed with ice-cold 0.9% NaCl, blotted on filter paper and frozen at once. It was necessary to pool 4 to 5 of the hearts from fetal animals (from the same litter) to provide sufficient tissue for one single norepinephrine and epinephrine determination. The new-born rabbits were decapitated either just at birth or later on, and the samples were prepared as with the fetuses. The tissue was homogenized in ice-cold 0.4 M perchloric acid by using a Tri-R tissue homogenizer (Genelab International) provided with a glass pestle. Homogenates were kept on ice until centrifuged at  $9,000 \times g$  at  $0^\circ\text{C}$  for 30 min. The residues were re-extracted twice more and all 3 supernatants were pooled<sup>5</sup>. The pH was adjusted to 8.5 with 0.5 M Tris buffer<sup>6</sup> and the samples were adsorbed onto alumina<sup>7</sup> (Merck Aluminium oxide active, acidic activity I), prepared by the method of ANTON and SAYRE<sup>8</sup>. The

alumina containing the adsorbed catecholamines was washed with bi-distilled water. After centrifugation, the supernatant was carefully aspirated off. Elution was performed with  $3 \times 2 \text{ ml}$  of 0.3 N acetic acid which was thoroughly mixed with the alumina by using a magnetic stirrer. All 3 eluates were pooled, centrifuged, adjusted to pH 6.5 and used for fluorometric assay<sup>9</sup>. For fluorometric measurement, an Aminco-Bowman Spectrofluorimeter with ellipsoidal mirror was used. Readings were made at activation wave lengths of 380 and 430 nm and at fluorescence wave lengths of 490 and 540 nm. The mean values  $\pm$  SEM are given in ng/g and ng/single heart. The *t*-test was computed.

**Results.** In the 30- and 31-day-old fetal rabbit heart (gestational age), the norepinephrine level is low. As no change was observed from one day to another, we have pooled the values. Their mean value is  $85 \pm 12 \text{ ng/g}$ , as can

<sup>1</sup> G. S. DAWES, in *Foetal and Neonatal Physiology* (Year Book Medical Publ., Chicago 1969), p. 117.

<sup>2</sup> J. ROFFI, J. L. FROGER and M. F. DEBRAY, *C. r. Acad. Sci., Paris* 287, 595 (1973).

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<sup>4</sup> K. OKYAYUZ and R. GHAMRIR, *Experientia* 29, 1472 (1973).

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<sup>6</sup> J. P. HANIG, J. M. MORRISON and S. KROPS, *Analyt. chim. Acta* 59, 363 (1972).

<sup>7</sup> V. RENZINI, C. A. BRUNORI and C. VALORI, *Clin. chim. Acta* 30, 587 (1970).

<sup>8</sup> A. H. ANTON and D. F. SAYRE, *J. Pharmac. exp. Ther.* 138, 360 (1962).

<sup>9</sup> U. S. VON EULER and F. LISHAJKO, *Acta physiol. scand.* 51, 348 (1961).

be seen in Figure 1. About the same level was found at parturition. Then, suddenly, within 1 to 4 h, the level of norepinephrine increases to  $145 \pm 16$  ng/g ( $p < 0.005$ ). At a more advanced age (33–72 h), the mean value reaches  $154 \pm 18$  ng/g. A similar evolution can be seen when the values are expressed in ng/single heart.

The epinephrine level is very low as compared to norepinephrine: 5 to 6-fold less in the fetus and at parturition, down to 14-fold at a more advanced age (see Figure 2). In the fetal period, the mean value is  $17 \pm 4$  ng/g and

declines to  $13 \pm 4$  at parturition. After 1 to 4 h and even after 3 days, the level still remains very low ( $10 \pm 2$  and  $11 \pm 1$  ng/g). Only a slight change was noticed when the mean values were expressed in ng/single heart.

**Discussion.** It has been shown that endogenous levels of catecholamines are low in the fetal and new-born animals of some species<sup>10–12</sup>. The concentration of cardiac norepinephrine was found to be low in the fetal period (late term) and also at parturition. At a more advanced age (2–3-day-old animals), the level was 80% higher. This increase may be explained by a progressive maturation of postganglionic sympathetic innervation of the rabbit heart. Relatively high levels attained rapidly within 1 to 4 h after parturition could be due to an increase in biosynthesis and also to uptake. In the adrenals of rabbit fetus, the catecholamine concentration rises progressively during the 3rd term of the fetal period<sup>3</sup> and declines to about 50% within 4 h after parturition<sup>2</sup>. Plasma norepinephrine level is high at parturition in new-born rabbits and decrease between 4–8 h after birth<sup>4</sup>. The heart of the new-born rat at the age of 1 to 8 days is unable to bind <sup>3</sup>H-norepinephrine as well as does the adult heart<sup>13</sup>. As no similar research has been done on the new-born rabbit heart, we do not know exactly if and how much norepinephrine can be bound just after birth. It is possible that the new-born rabbit heart is able to take up, at least temporarily, some of the norepinephrine present in the plasma, which declines after parturition. If so, only the norepinephrine was bound and not the epinephrine, which does not increase in the heart after birth.

It is not sure that the relatively high concentration of norepinephrine found in the new-born heart within 1 to 4 h after parturition is absolutely necessary for its activity. In the adult animals, the role played by endogenous norepinephrine, e.g. on cardiac contractility, is still controversial<sup>14</sup>. It has been suggested that adrenal release of catecholamines in the new-born animals could play a critical role in stimulating the cardiovascular response to asphyxia and initiating respiration at birth<sup>15</sup>. The sudden increase of cardiac norepinephrine a few hours after parturition supports this hypothesis<sup>16</sup>.

**Résumé.** Chez le Lapin nouveau-né, le taux de la noradrénaline cardiaque s'élève brusquement, doublant presque pendant les 4 heures qui suivent la parturition.

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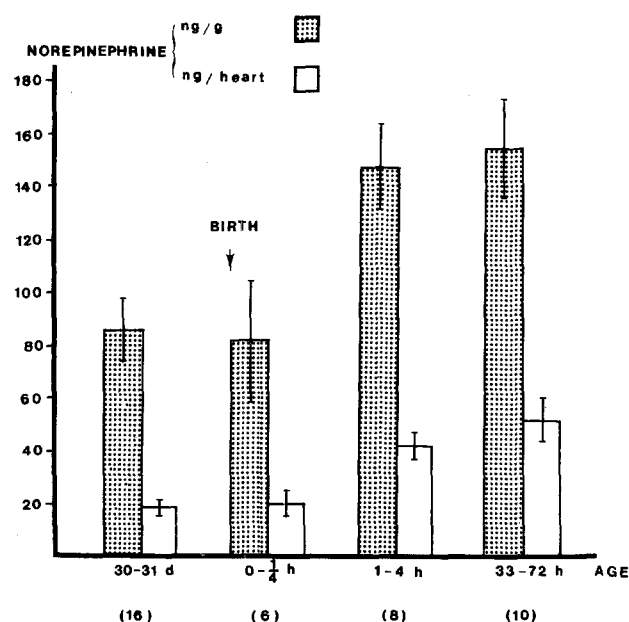


Fig. 1. Norepinephrine level in fetal and neonatal rabbit heart. Mean values and standard error for each age group are given. The number of samples is indicated in parenthesis.

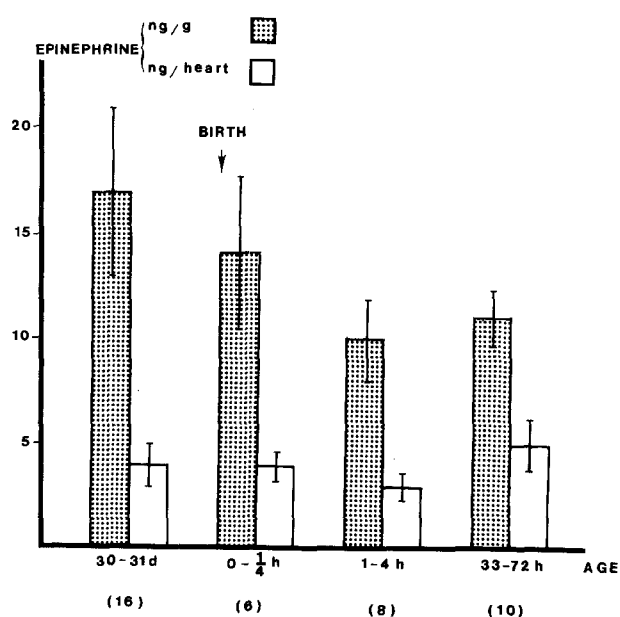


Fig. 2. Epinephrine level in fetal and neonatal rabbit heart (for legend, see Figure 1).

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