Creatine Kinase in Serum after Uterus Contraction Produced by Oxytocin

It has been reported by others, and confirmed by our own observations that creatine kinase is increased in serum immediately after delivery[1,2]. However, it is not known if the observed modification is due to the contractions of the uterus or to the contractions occurring in the striated muscle during labour. Therefore the phenomenon has been investigated again, measuring creatine kinase in human serum before and after uterus contraction produced by oxytocin.

Creatine kinase has been determined in the serum of 6 women subjected to Caesarean section before operation and 1 h after uterine contraction elicited by i.v. injection of 5 U of synthetic oxytocin (Sandoz, Basel); in 3 women on the ninth day after total hysterectomy and bilateral salpingo-oophorectomy, also before and after administration of oxytocin; and in 4 women before and after a gynaecological operation. Creatine kinase was assayed with the method of ENNOR and ROSEMBERG[3], as modified by HUGHES[4], in serum obtained centrifuging heparinized blood.

Creatine kinase in human serum before Caesarean section and 1 h after treatment with oxytocin

Case	μmoles creatine phosphor./l serum/h	
	before	after
1	26.2	106
2	11.0	60
3	11.2	54
4	11.0	48
5	16.4	50
6	13.2	60

In all cases administration of oxytocin to women subjected to Caesarean section gives rise to a marked increase of serum creatine kinase. In the cases in which uterus has been previously removed, treatment with oxytocin has no effect on serum creatine kinase. During other gynaecological operations, where there is no uterine contraction, only slight modifications are observed.

From the results obtained it may be concluded that a prolonged contraction of the uterine muscle gives rise to a high increase of serum creatine kinase.

Riassunto. In donne sottoposte a taglio cesareo la contrazione dell'utero provocata da ossitocina causa un netto aumento della creatinacinasi del siero. Con lo stesso trattamento con ossitocina l'enzima non varia in donne prive di utero.

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Signs of Cerebral Hypoxia in Hyperventilation

Although measurements of cerebral circulation (CBF), cerebral electrical activity or cerebral O_2 tension during marked hyperventilation suggest that the CBF is reduced to a degree which leads to cerebral hypoxia[1,2], conclusive proof thereof has been lacking. Such proof evidently requires measurements of the redox state of suitable intracellular redox systems[3,4]. In the present paper a report is given on measurements of cerebrospinal fluid (CSF) and cerebral tissue concentrations of lactate and pyruvate during varying degrees of hyperventilation in anaesthetized cats. These results suggest the presence of cerebral hypoxia at arterial CO_2 tensions below 20 mm Hg.

Methods. Cats were anaesthetized with i.p. phenobarbital (100 mg/kg) and tracheotomized. Arterial samples were withdrawn anaerobically from a cannula in one femoral artery, and CSF samples from the suboccipital cistern. Arterial blood was analyzed for pH and P_{CO_2}[5]. Blood and CSF were collected directly in liquid nitrogen for the subsequent enzymatic analysis of lactate and pyruvate. After taking at least 2 control blood and CSF samples, the animals were either hyperventilated for 60–90 min, or were allowed to breathe 9–15% CO_2 for the same time periods. At the end of the experiments, the brain tissue was frozen in situ with liquid nitrogen which was poured directly onto the exposed dura. The subdural tissue was then chiselled out and the lactate and pyruvate concentrations analyzed enzymatically[6].

Results. In the Figure, the arterial CO_2 tension has been plotted against the CSF lactate concentration and against the CSF lactate/pyruvate ratio. There is a marked increase in the CSF lactate concentration when the arterial CO_2 tension is brought below 20–25 mm Hg. At the same CO_2 tensions, the CSF lactate/pyruvate ratio is progressively increased. Essentially the same results were obtained on the brain samples, showing that the direction of changes was the same in both extra- and intracellular spaces, although the lactate and pyruvate concentrations differ between the 2 compartments.

Discussion. It has been pointed out that since the lactate/pyruvate system is coupled to the NADH/NAD^+

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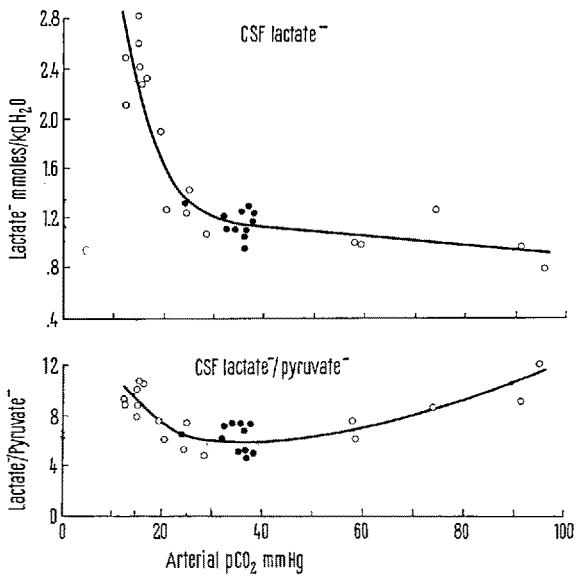
system, analyses of lactate/pyruvate ratios in cellular or extracellular systems might give important information on the redox state of the cells[3,4,7]. However, the steady state relation between the systems involves hydrogen ions

$$\frac{NADH}{NAD^+} = \frac{(Lactate)}{(Pyruvate)} \cdot \frac{K}{(H^+)}$$



The relation between the arterial CO_2 tension and the lactate concentration and the lactate/pyruvate ratio of cisternal CSF in anaesthetized and immobilized cats. The animals were either spontaneously breathing air or 7–9% CO_2, or they were mechanically hyperventilated for 60–90 min. Control samples are denoted by filled circles. Note increased lactate/pyruvate ratio at CO_2 tensions below 20–25 mm Hg.

where K is the equilibrium constant. The equation shows that at a constant redox state the lactate/pyruvate ratio will vary directly with the hydrogen ion concentration. Thus, we would expect the lactate/pyruvate ratio to increase in hypercapnia (see Figure) and decrease in hypocapnia. The fact that the lactate/pyruvate ratio increases during hyperventilation thus suggests an increased NADH/NAD^+ ratio, i.e. a state of hypoxia (cf. ref. [8] and [9])[10].

Zusammenfassung. Passive Hyperventilation anästhesierter und immobilisierter Katzen führt zu signifikanter Erhöhung des Laktat-Pyruvat-Quotienten in Zerebrospinalflüssigkeit und Gehirngewebe. Wegen der Verbindung zwischen Laktat/Pyruvat- und NADH/NAD^+-System ist somit anzunehmen, dass Hyperventilation (CO_2-Druck unter 20–25 mm Hg) zu zerebraler Hypoxie führt.

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Influence of a Mixture of Radioprotectors on the Mucosa of the Small Intestine of Mice Irradiated with 2000 R of X-Rays

Intestinal death occurs from the third to the fifth day after doses of 1–10 kR and is preceded by inhibition of cell division, destruction of the crypts, shortening of the villi and denudation of the intestinal epithelium (QUASTLER[1], MAISIN[2]). Mixtures of chemical protectors offer a better protection to the stem cells in the duodenum of mice than the most patent sulfhydryl radioprotectors given alone (MAISIN[2,3], MAISIN and MATTELIN[4]). The present communication reports data on the influence of mixtures of radioprotectors on the stem cells of the duodenum of mice during a period of 30 days after a dose of 2000 R of X-rays.

Materials and methods. Twelve-week-old male mice of the BALB/c strain weighing 25–30 g were used. The treated mice were given 16 mg of reduced glutathione by stomach tube 25 min before irradiation with 2000 R of X-rays (300 kV, 20 mA, 1mm Al, 2 mm Cu; dose rate 100 R/min). Fifteen min later, the mice were injected i.p. with 15 mg of cysteine and 10 mg of AET (both neutralized to pH 7.2 with NaOH) and, 20 min after administration of glutathione, with 1 mg of serotonin creatinine sulphate. The number of nuclei, mitoses, karyorrhexis and pycnosis were determined in at least 75 crypts/time point. The mice were killed by cervical dislocation at various time intervals after X-ray exposure. The duodenum was fixed in Bouin or neutral formaline, or in Carnoy. Slices were stained with hematoxylin eosine or with Feulgen.

Results and discussion. On the first day after exposure to 2000 R of X-rays, some cellular debris and fewer, often abnormal, mitoses are visible, but otherwise the mucosa of the duodenum appears normal. On the third day the crypts are atrophic and irregular, most of the villi have a normal aspect. Seven days after irradiation, some crypts are still atrophic, others are irregular and deeper than normal; the villi appear normal. From the ninth to the thirtieth day, the mucosa of the duodenum regains its normal aspect.

The number of the nuclei in the crypts column is presented in Figure 1. In the irradiated protected mice, the number of the nuclei decreases until day 2 (38% of the

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