EFFECT OF EXCLUSION OF PULMONARY RESPIRATION ON A FROG'S HEART UNDER CONDITIONS OF POISONING OF COUPLED PHOSPHORYLATION

I. P. Lapin

From the Dept. of Pharmacology (Chairmn: V. M. Karasik, Corresponding Member Acad. Med. Sci. USSR), Leningrad Pediatric Medical Institute (Director: N. T. Shutova).

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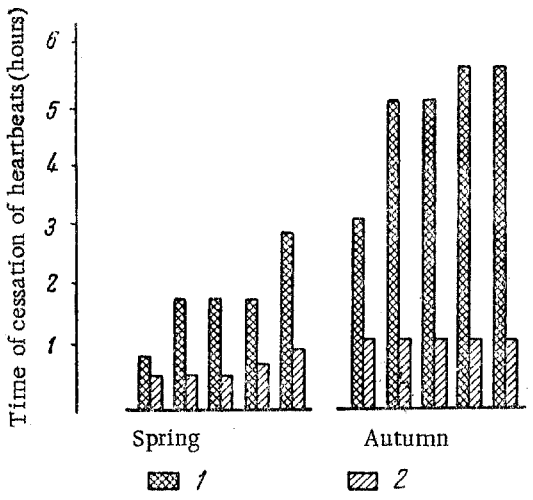
While making an electrocardiographic study of the effect of 2, 4-dinitrophenol on the heart of a frog we found that exclusion of pulmonary respiration by administration of curare greatly enhanced the effect of dinitrophenol. Inasmuch as the frog takes in less oxygen when pulmonary respiration is excluded, it may be considered to be in a state of hypoxia. It is known that tolerance of animals to hypoxia is lowered under conditions of poisoning of respiratory phosphorylation [1, 3]. In the experiments described below, performed on 158 frogs, we studied the effect of combining hypoxia caused by exclusion of pulmonary respiration with poisoning of oxidative phosphorylation.

Effect on a Frog's Heart of Exclusion of Pulmonary Respiration by Curarization, Under Conditions of Poisoning with 2, 4-Dinitrophenol

Time of arrest of heart	Spring	Autumn
At the end of the 3rd hour	22	3
" " " " 4th hour	–	20
After 4 hours	–	14
Total	22	37

Together with peripheral exclusion of pulmonary circulation by the action of curare (118 frogs) we also studied central abolition of respiration caused by urethane narcosis (40 frogs). We found that urethane also greatly intensifies the effect of dinitrophenol on the heart. The similarity between the effects produced by curare and urethane, which differ in structure and in their mode of action, can, under the given experimental conditions, be due to the only effect which they have in common, viz., to abolition of pulmonary respiration. Curarization or urethane poisoning, causing paralysis of the respiratory muscles, or introduction of dinitrophenol in the given dosage (10-20 γ per g body weight), caused only slight retardation of heart beat (46 control frogs, of which 26 received dinitrophenol). When the same doses of dinitrophenol were given together with curare or urethane we observed progressive retardation of the pulse rate, with terminal arrest of the heart in diastole in all the animals without exception; contraction of the ventricles followed after 30-60 minutes. Exclusion of pulmonary respiration of spring frogs was followed by cessation of heart beat much sooner than with autumn frogs (see Table). This finding is in accordance with Krogh's finding [2] that heightened oxygen requirement in the spring months is met chiefly by pulmonary respiration. A comparison of the effects of different procedures for abolishing pulmonary respiration on the action of the heart in poisoned frogs showed that cardiac arrest occurs 3-4 times faster in urethane narcosis than with curarization (see Figure). This phenomenon requires further examination.



Time of arrest of frogs' hearts after administration of 2,4-dinitrophenol, applying different ways of abolishing pulmonary respiration (results of 4 experiments, using 5 frogs for each). 1) Curarization, 2) urethane narcosis.

Our attention was directed in the above experiments primarily to changes in the action of the heart. We noticed, however, that stiffening of the skeletal muscles took place in spring frogs prior to arrest of the heart; this was never seen in autumn frogs.

Use is made of metabolic poisons in the study of oxidative phosphorylation, which is of great biochemical importance as a source of production of high energy phosphate bonds. In this connection tests of the efficacy of poisons suppressing oxidative phosphorylation are of importance. The great simplicity of the experimental methods described above permits of the utilization of cardiac arrest in frogs with abolished pulmonary respiration and with toxic uncoupling of oxidative phosphorylation as one of these tests.

LITERATURE CITED

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