In the early period of resuscitation after circulatory arrest for 15 min in dogs the rate of metabolic clearance of 17-hydroxycorticosteroids (17-HCS) was found to be reduced, more especially in animals which subsequently died. This decrease was due mainly to a decrease in the clearance of plasma 17-HCS by organs in the splanchnic region and was evidently connected with the circulatory disturbances.

KEY WORDS: circulatory arrest; postresuscitation period; rate of metabolic clearance of 17-hydroxycorticosteroids.

Increased secretion of certain adaptive hormones in various types of stress and terminal states has recently been conclusively proved, but the problem of coexisting changes in hormone utilization in the body still remains unexplained. The most complete picture of the uptake of hormones by effector tissues is given by the rate of metabolic clearance of the hormone, reflecting the volume of plasma irreversibly freed from hormone in unit time [11]. Its value, according to various workers [4, 9, 12, 13], correlates directly with the strength of the hormonal effect.

Changes in the rate of metabolic clearance of cortisol in the postresuscitation period after circulatory arrest for 15 min were studied.
EXPERIMENTAL METHOD

Experiments were carried out on 34 anesthetized (pantopon 4 mg/kg, pentobarbital 10-25 mg/kg), heparinized (100 i.u./kg) dogs weighing 15-30 kg. In control experiments (11 dogs) the possibility of using the method of determining the rate of metabolic clearance of cortisol (RMCC) was studied. For this purpose, the RMCC was determined repeatedly in five experiments at intervals of 1-2 h, in another three experiments its changes were studied after abolishing the secretion of endogenous hormones by adrenalectomy, and in a further three experiments after a test laparotomy. In the experiments of group 1 (11 dogs) the RMCC was investigated in the initial state and during 1-6 h of the recovery period after circulatory arrest for 15 min caused by electric shock [2]. In the experiments of group 2 (10 dogs) the extrasplanchnic RMCC was determined. For this purpose, the vessels of the liver, spleen, pancreas, and gastrointestinal tract were ligated in six animals just recovering from circulatory arrest. In four experiments of group 2 a similar operation was performed on animals in which a terminal state had not been produced. In addition, in two animals the RMCC was reinvestigated during hypovolemic hypotension for 5 h to a level of 60-90 mm Hg and a reduction of the cardiac output to 45 ± 5% of its initial value in order to determine the role of circulatory disturbances in hormone utilization. The RMCC was determined by a method of single loading with the hormone [7, 8, 11]. Through an arterio-venous shunt of the femoral vessels the animals received cortisol sodium hemisuccinate in a dose of 1 mg/kg over a period of 1 min. The concentration of free 17-hydroxycorticosteroids (17-HCS) in the plasma [3] was determined before and 30, 60, 90, and 120 min after loading. The rate of metabolic clearance of 17-HCS was calculated from the monoexponential curve of disappearance of the injected cortisol.

EXPERIMENTAL RESULTS

During repeated determinations in the control dogs no significant change was found in the rate of metabolic clearance of 17-HCS (17.7 ± 3.3 and 16.3 ± 2.4 ml/min·kg). Adrenalectomy and laparotomy increased this figure equally (by 45-50%; P < 0.05). The control experiments thus confirmed that the method can be used and their results also indicated a change in the index under stress conditions, in agreement with data in the literature [5-7, 10].

Depending on the results of resuscitation after circulatory arrest for 15 min the animals of group 1 were divided into two subgroups: those which survived and those which died during the first 24 h. In the five dogs which survived stable cardiac activity was restored sooner (on average by 3 min; P < 0.05), but the recovery time of certain other functions (respiration, corneal and spinal reflexes) did not differ significantly from that in animals which died during the first 24 h of the experiments. Between the first and sixth hours of the postresuscitation period, the rate of metabolic clearance (RMC) of 17-HCS fell by 35% below its initial level in the dogs which died (P < 0.05) but by only 10% in those which survived. The plasma 17-HCS level before cortisol loading was the same before the experiment and after resuscitation in both the surviving and the dying dogs, namely 16.1 ± 1.4, 16.2 ± 1.4, and 15.8 ± 2.4 µg% respectively. On the basis of the plasma endogenous 17-HCS level before loading and their RMC, the production of endogenous 17-HCS was calculated. It was 1.9 ± 0.2 µg/min·kg before the experiment, compared with 1.4 ± 0.2 after resuscitation in the dying dogs and 2.0 ± 0.1 µg/min·kg in the survivors. The differences between the values for the subgroups were statistically significant (P ± 0.02).

The decrease in RMC of 17-HCS in the early postresuscitation period can be attributed both to hypoxic injury to specific tissue receptors of the hormones and to the development of a low cardiac output syndrome, which was most marked in the nonviable animals [1]. In fact, in the experiments with hypovolemic hypotension accompanied by a sharp fall in cardiac output the RMC of 17-HCS was 42% lower than initially.

Since glucocorticoids are utilized by virtually all tissues of the body, the question naturally arose: Which tissues are mainly responsible for the change in the total RMC of 17-HCS during resuscitation? In control "eviscerated" animals the rate of extrasplanchnic 17-HCS clearance was 11-17% of the total rate of this process. In the postresuscitation period in 4 of 6 experiments on "eviscerated" animals it reached almost 40% of the total rate, and only in one experiment was it a lower percentage than in the control.

Consequently, in the postresuscitation state the total rate of 17-HCS clearance was reduced on account of a sharp decrease in the role of organs of the splanchnic region in that process, whereas the 17-HCS clearance by extrasplanchnic tissues was evidently actually increased.