effects in the action of extracts of whole spinal cord (Tables 1 and 2) indicates the possible neurochemical basis of asymmetry of segmental reflexes.

The ability of extracts of halves of the brain [2, 5, 7] and spinal cord (Tables 1 and 2) to induce effects confined to the homonymous side of the spinal cord is proof that the distribution of LF in these two parts of the CNS is similar in principle of distribution of LF in the nervous system, reflecting the similarity of peptide composition of brain and spinal cord LF and the identical direction of changes in peptide concentrations in several situations, taken together, explain the hitherto unexplained fact that in vestibulopathy asymmetry of muscle tone of the recipient's hind limbs is caused by extracts not only of the spinal cord (Tables 1 and 2), but also of the brain [6]. Asymmetry of the effects of LF is perhaps linked with asymmetry of opiate receptors, as is shown by abolition of the action of LF in the presence of the opiate antagonist. This hypothesis is in agreement with data on asymmetrical changes of muscle tone under the influence of opioid peptides [1, 4].

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EFFECT OF VITAMIN E DEFICIENCY ON CARDIAC ARRHYTHMIAS INDUCED BY ACUTE ISCHEMIA

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KEY WORDS: acute ischemia; cardiac arrhythmias; vitamin E deficiency; lipid peroxidation.

Recent investigations have shown that activation of lipid peroxidation (LPO) due to stress, acute ischemia [2], and also direct induction of LPO [4] in the isolated atrium lead to injury to cardiomyocyte membranes and may thus play a role in the genesis of cardiac arrhythmia and fibrillation, which are prevented by synthetic antioxidants [2, 4]. In this connection it seemed probably that a deficiency of the principal natural antioxidant and membrane stabilizer, α-tocopherol (TP), may reduce the resistance to the heart to arrhythmias and fibrillation, that frequently arise in response to acute ischemia and which constitute the main cause of sudden death.

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TABLE 1. Effect of Vitamin E Deficiency on DMA Level and Development of Arrhythmias in Acute Ischemia

Experimental conditions	MDA concentration in myocardial homogenate, μmoles/g	Number of animales with arrhythmias	Arrhythmias during 10 min of acute ischemia						Total duration of arrhythmias, sec	
			fibrillation		ventricular tachycardia		extrasystoles			
			number of animals	duration, sec	number of animals	duration, sec	number of animals	duration, sec	for one animal	for whole group
Control (n =11)	0,395±0,022	11	0	0	5	2,5±1,0	11	20±3,8	20±4,2	220
Vitamin E deficiency (n =11)	0,606±0,068	11	3	77±60	10	15,8±4,8	10	27±6,5	50±9,0	658
P	<0,05		—	<0,001	—	<0,05	—	>0,1	<0,01	

The aim of this investigation was to test this hypothesis by comparing the frequency of arrhythmias and the concentration of an LPO intermediate, namely malonic dialdehyde (MDA), during acute ischemia induced in control animals and in a parallel series of animals with alimentary vitamin E deficiency.

EXPERIMENTAL METHOD

Experiments were carried out on male Wister rats weighing 250-300 g. Animals initially weighing 60-80 g were kept for 2 months on a diet of the following composition: casein 22%, starch 60%, linetol 3%, lard 7%, filter paper (as cellulose) 3%, mixed salt 4%, mixture of water-soluble vitamins 0.1%. The compositions of the mixed salt and mixture of vitamins are given in [5]. The animals were divided into two groups: rats receiving an optimal vitamin E supply (control), to whose diet α-tocopherol acetate was added in the proportion of 100 mg per kilogram of food, and rats with vitamin E deficiency, to whose diet this vitamin was not added.

The degree of the adequacy of the vitamin E intake of the animals was judged by the serum TP concentration, which was measured fluorometrically [6]. The serum TP concentration of the control animals was found to be 1.03 ± 0.05 mg/100 ml, whereas in rats kept on a diet without vitamin E it was 0.070 ± 0.011 mg/100 ml.

The experiments were done in June. Acute ischemia was induced under urethane anesthesia (160 mg/kg) and the animals were artificially ventilated with air. After thoracotomy a ligature was introduced beneath the point of origin of the descending branch of the left coronary artery, and this was then tightened. The zone of irreversible ischemia and subsequent necrosis produced by this method is about 50% of the weight of the left ventricle [3]. The severity of the arrhythmias in these experiments was assessed by the ECG, which was recorded in three standard derivations on a Mingograf-34 apparatus (Siemens-Elema, Sweden). The heart was quickly removed 10 min after development of ischemia, washed free from blood, and frozen in liquid nitrogen. The MDA concentration was determined in the ventricular myocardium by the method in [8].

EXPERIMENTAL RESULTS

Two hypotheses can be put foward on the basis of the data given in Table 1. First, avitaminosis E led to an increase in the MDA (product of LPO) concentration in the animals' heart muscle by 53%. Second, in animals with vitamin E deficiency and with marked activation of LPO, assessed by measuring the quantity of DMA which accumulated, the heart responded to acute ischemia with arrhythmias of much higher frequency and greater severity than in the control. The total duration of all arrhythmias, calculated per animal and for each group compared, was increased more than twofold in vitamin E deficiency.

On the whole the results indicate that in deficiency of the principal natural antioxidant, TP, activation of LPO takes place, with elevation of the MDA level by 50%, accompanied by a significant increase in the probability of appearance of arrhythmia and fibrillation of the heart during acute myocardial ischemia. This result is in harmony with recent ideas of the role of LPO in the pathogenesis of arrhythmias [2, 4], and it explains the arrhythmogenic effect of vitamin E deficiency by diminution of its antioxidant action.

Meanwhile the membrane-protective action of TP cannot be reduced simply to limitation of LPO. It has been shown that TP is able to bind fatty acids and lysophosphatides [1]. It can

accordingly be postulated that injury to cardiomyocyte membranes in vitamin E deficiency, accompanied by lowering of the electrical stability of the heart, is realized not only through activation of LPO, but also on accounts of the effect of arrhythmogenic factors such as fatty acids and lysophosphatides [7, 9]. This hypothesis requires experimental verification.

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SARCOLEMMAL DAMAGE AS A PATHOGENETIC FACTOR OF PITUITRIN-ISOPRENALINE-INDUCED MYOCARDIAL ISCHEMIA AND ITS CORRECTION BY AN ANTIOXIDANT (DIBUNOL)

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Correlation between disturbance of functional and structural integrity of the sarcolemma and myocardial function has recently been reported. It has been shown, in particular, that in ischemic and hypoxic myocardial damage the state of the sarcolemma determines whether or not the reversible intracellular changes becomes irreversible [6, 8]. Sarcolemmal damage has been shown to be one of the principal factors in the development of acute heart failure [5]. By the use of peroxidase and ferritin as intravital tracers, disturbance of the structure of the cardiomyocyte sarcolemma has been demonstrated under the influence of toxic doses of catecholamines [11, 12]. An important role in maintenance of normal membrane function is played by lipid peroxidation (LPO). By auto-oxidation of catecholamines, free radicals are formed [13], which oxidize polyunsaturated fatty acids of membrane phospholipids. Intensification of LPO has been described in isoprenaline-induced myocardial necrosis, and prophylactic administration of the bioantioxidant tocopherol has been observed against the action of toxic doses of isoprenaline [14, 15].

The aim of this investigation was to study the state of the myocardial and erythrocyte membranes in pituitrin-isoprenaline-induced myocardial ischemia (PIMI), the role of lipid peroxidation in injury to these membranes, and the membrane-protective action of the synthetic antioxidant dibunol (2,6-di-tert-butyl-4-methylphenol).

EXPERIMENTAL METHOD

Experiments were carried out on 43 non-bred albino rats aged 24-30 months and weighing 350-500 g. Pituitrin (15 U/kg) and isoprenaline (100 mg/kg) were injected intraperitoneally in two doses with an interval of 24 h. The state of the membrane was evaluated 24 h after the second injection of isoprenaline and pituitrin, by determining passive penetration of sulfacetamide sodium into the myocardium (the ratio of the sulfacetamide sodium concentra-

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