the first experiment triacetin could not replace acetate salts in the diet and butyrate could be omitted. Butyrate was found present in the same amount in the rumen contents irrespective of its presence in the diet. The second experiment showed growth could be obtained on simplified diets supplying energy as carbohydrate or triacetin if sodium and/or potassium were added to the ration.

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Role of Sodium in Production of Myocardial Necroses by Stress.* (24505)

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Previous experiments have shown that, following prolonged pretreatment with large doses of certain corticoids, *e.g.*, 2α-methyl-9α-chlorocortisol (Me-Cl-COL), a brief period of neuromuscular effort (induced by forced restraint) can elicit acute, massive myocardial necroses in the rat(1). Subsequent investigations revealed that the precipitating effect of neuromuscular effort is not specific, since a variety of other stressors (hot or cold baths, surgical trauma, adrenaline) also produce myocardial necroses after conditioning with Me-Cl-COL. It was found, furthermore, that certain sodium salts (phosphates, sulfates, perchlorate) can, while others (chloride, acetate, citrate, lactate) cannot replace the stressors in precipitation of myocardial necroses after Me-Cl-COL conditioning(2). No salts of cations other than Na were effective, but these observations show that the anion also plays an important role in the pathogenesis of this type of myocardial necrosis. We were particularly impressed by the fact that, although NaCl and the organic Na-salts were almost always totally ineffective after Me-Cl-COL-pretreatment, they occasionally produced very pronounced cardiac necroses, in rats damaged through fortuitous circumstances. It was, therefore, postulated that, after suitable sensitization with corticoids, certain Na-salts (phosphates, sulfates, perchlorate) produce cardiac necroses under ordinary conditions, while others (chloride and several organic salts) are inactive in themselves, but become highly effective during stress. We now wish to report upon experiments which substantiate this concept.

Materials and methods. Two hundred female Sprague-Dawley rats, with mean initial body weight of 100 g (range: 95-110 g), were subdivided into 20 equal groups, as indicated in Table I. Me-Cl-COL† was administered subcutaneously, in the form of its acetate, as a microcrystal suspension of 100 μg in 0.2 ml of water, once daily. All the Na-salts were given by stomach tube, at the dose of 2 mM, in 2 ml of water, twice daily. Neuromuscular stress was induced by maintaining the rats on a board with adhesive tape, for a period of 17 hours, on the fifth day of the experiment. The animals of all groups were killed with chloroform on the sixth day. The hearts were fixed in neutral formalin and embedded in paraffin for subsequent staining with our fuchsin technic(2). The intensity of the necroses was assessed in terms of an arbitrary scale of 0-3, and the means of these readings (with standard errors) are listed in Table I.

Results. It is evident from our data that, in these rats, cardiac necroses do not occur

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TABLE I. Role of Sodium in Production of Myocardial Necroses by Stress in 20 Groups.

Treatment	Cardiac necroses
None	0
NaCl	0
Na-Acetate	0
-Citrate	0
-Lactate	0
Me-Cl-COL	0
+ NaCl	0
+ Na-Acetate	.1 ± .10
+ -Citrate	0
+ -Lactate	.2 ± .20
Restraint	.1 ± .10
+ NaCl	.1 ± .10
+ Na-Acetate	.2 ± .20
+ -Citrate	.1 ± .10
+ -Lactate	.1 ± .10
+ Me-Cl-COL	.4 ± .18
+ " + NaCl	1.9 ± .14
+ " + Na-Acetate	2.6 ± .30
+ " + -Citrate	2.1 ± .25
+ " + -Lactate	3.0 ± .0

spontaneously (Group 1), or after treatment with any of the Na-salts (Groups 2-5) or Me-Cl-COL alone (Group 6). Treatment with Me-Cl-COL + Na-salts (Groups 7-10), restraint alone (Group 11) or restraint + Na-salts (Groups 12-15) produced only minute necrotic foci in occasional animals. These lesions were never large enough to be detectable by the naked eye or the hand loupe. Combined treatment with restraint + Me-Cl-COL (Group 16) was somewhat more effective, but (owing to the low dosage of Me-Cl-COL) even here the lesions were very small and only occasionally visible under loupe magnification. By contrast, in the animals treated with restraint + Me-Cl-COL in combination with the otherwise ineffective Na-salts (Groups 17-20), pronounced cardiac necroses were invariably detectable by naked-eye inspection, because they affected large areas of the myocardium. Deaths occurred only among the rats treated with restraint + Me-Cl-COL combined with either Na-citrate (40% mortality, Group 19) or Na-lactate (10% mortality, Group 20).

Discussion. The principal outcome of these experiments is that certain Na-salts (ineffective in themselves and during simultaneous treatment with either Me-Cl-COL or a stressor) become highly effective in producing massive myocardial necroses, when given in combination with Me-Cl-COL and a stressor, such as forced restraint. Further studies will be necessary to elucidate the mechanism through which otherwise ineffective Na-salts can produce acute myocardial necroses in Me-Cl-COL-conditioned rats during restraint. It is also still uncertain whether there exists any close pathogenetic relationship between the experimental cardiac necroses thus produced and the acute cardiac infarcts that occur in man. It is significant, however, that both these conditions can be elicited by an acute stress situation.

Summary. Certain Na-salts (chloride, acetate, citrate and lactate) are well tolerated even by rats simultaneously treated with 2α-methyl-9α-chlorocortisol (Me-Cl-COL) or a severe stressor, such as forced restraint. However, these same salts produce massive and sometimes fatal myocardial necroses, in rats exposed to the stress of forced restraint after conditioning with Me-Cl-COL. It appears that during stress the metabolism of certain otherwise innocuous Na-salts and/or steroids is so altered that they acquire severe cardiotoxic properties.

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