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Production by Various Fats of Myocardial Necroses in Humorally Conditioned Rats.* (23940)

HANS SELYE

Institut de Médecine et de Chirurgie expérimentales, Université de Montréal, Montréal, Canada

When rats are simultaneously treated with certain highly active corticoids, such as 2α-methyl-9α-chlorocortisol (Me-Cl-COL)† plus sodium phosphates (Na_2HPO_4, NaH_2PO_4), they invariably succumb with clinical manifestations of acute cardiac death, and autopsy regularly reveals large, yellowish infarct-like necrotic patches in their myocardium(1). Exposure to stress (*e.g.,* neuromuscular exertion) can precipitate the development of such infarct-like myocardial necroses, in rats conditioned by pretreatment with small doses of corticoids and electrolytes(2). These cardiac lesions are not accompanied by any morphologically demonstrable evidence of coronary artery occlusion, yet they resemble cardiac infarcts in some respects. Since, during the last few years, a great deal of evidence has accumulated in support of the concept that certain fats may precipitate the development of true cardiac infarcts in man(3), we wanted to verify whether the production of myocardial necroses by corticoids plus sodium phosphate in the rat could likewise be precipitated by the oral administration of fats.

Materials and methods. One hundred forty female Sprague-Dawley rats, with an average initial body-weight of 99 g (range: 93-109 g), were subdivided into 14 equal groups as indicated in Table I. Me-Cl-COL was injected subcutaneously, in the form of its acetate, as a micro-crystal suspension of 100 μg in 0.2 ml of water, once daily. Na_2HPO_4 was administered by stomach tube, at the dose of 1 mM (141.98 mg) in 5 ml of water, twice daily. The various fats were given twice daily, by stomach tube, at the doses indicated in Table I. The experiment was terminated after 6 days, by killing the survivors with chloroform. The hearts of all animals were fixed in Susa solution, for subsequent staining with hematoxylin-eosin. Since nephrocalcinosis frequently accompanies the myocardial necroses produced by Me-Cl-COL plus Na_2HPO_4, specimens of all kidneys were fixed in neutral formalin for the subsequent histochemical demonstration of calcium deposits by the v. Kossa's silver nitrate technic. Both organs were embedded in paraffin.

Results. The principal results of these experiments are summarized in Table I, which lists the mean final body-weight, the severity (graded in terms of an arbitrary scale of 0 to 3) of cardiac necroses and nephrocalcinosis, as well as the percentual incidence of these changes, and the mortality rates.

Treatment with as much as 1 ml of corn oil, twice daily, alone (Group 1) or in com-

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TABLE I. Effect of Various Fats upon Myocardial Necroses.

Group	Treatment		Final body wt (g)	Cardiac necroses: Incidence (%)	Cardiac necroses: Grade (scale 0-3)	Nephrocalcinosis: Incidence (%)	Nephrocalcinosis: Grade (scale 0-3)	Mortality (%)
		ml						
1	Corn oil	1.0	94.5 ± 2.4	0	0	0	0	0
2	Me-Cl-COL + Corn oil	1.0	84 ± 2.1	0	0	0	0	0
3	Me-Cl-COL + Na_2HPO_4	5.0	82 ± 2.5	20	.5 ± .32	50	.6 ± .23	20
4	*Idem* + corn oil	.5	81 ± 2.3	80	1.7 ± .32	70	1.5 ± .40	30
5	" + "	1.0	82 ± 2.7	100	2.5 ± .25	89	1.7 ± .34	100
6	" + peanut oil	.5	83 ± 2.8	50	1.1 ± .44	60	.8 ± .28	20
7	" + "	1.0	80 ± 1.9	100	2.6 ± .27	80	1.0 ± .2	80
8	" + olive oil	.5	85 ± 2.1	60	1.6 ± .48	70	1.3 ± .37	40
9	" + "	1.0	84 ± 1.9	90	2.7 ± .30	100	1.9 ± .23	90
10	" + pork fat	.5	84 ± 2.8	60	1.6 ± .48	80	1.4 ± .34	40
11	" + "	1.0	80 ± 2.5	89	2.4 ± .38	89	2.1 ± .34	70
12	" + chicken fat	.5	83 ± 1.6	80	1.6 ± .34	80	1.6 ± .30	60
13	" + "	1.0	82 ± 1.6	100	2.9 ± .1	90	1.4 ± .23	100
14	" + paraffin oil	1.0	81 ± 1.8	10	.1 ± .1	30	.3 ± .15	10

bination with Me-Cl-COL (Group 2), produced no cardiac necroses, nephrocalcinosis or mortality. In these respects, Me-Cl-COL plus Na_2HPO_4, without additional treatment (Group 3), was also only very moderately effective because of the short duration of the experiment. This is in sharp contrast with the intensity of the cardiac necroses and nephrocalcinosis and with the high mortality rate in all the animals which, in addition to the steroid-electrolyte treatment, were also given plant or animal fats (Groups 4-13). On the other hand, the inabsorbable mineral oil did not significantly accentuate the production of organ changes, nor did it increase the mortality in rats concurrently treated with Me-Cl-COL plus Na_2HPO_4 (*cf.* Group 14 with Group 3).

The degree of nephrocalcinosis ran roughly parallel with the severity of the cardiac necroses.

Discussion. It would not be permissible to draw any definite conclusions from this experiment concerning the probable effect of various fats upon the incidence of true cardiac infarcts such as occur in man. It is clear, however, that under our experimental conditions, both plant and animal fats precipitated the production of myocardial necroses by short-term treatment with Me-Cl-COL plus Na_2HPO_4. This sensitization could not have been due to the stressor effect of daily gavages with oily material, since similar treatment with paraffin oil proved to be ineffective. Also, it is significant that the animals of all groups lost some body-weight during the experiment; hence, the fats could not have predisposed the cardiac muscle to the production of necroses, by placing, upon the heart, an excess burden due to an increase in body mass.

Summary. Experiments on rats indicate that the degree of myocardial necroses and nephrocalcinosis normally produced by combined treatment with 2α-methyl-9α-chlorocortisol (Me-Cl-COL) and Na_2HPO_4 is considerably increased by oral administration of plant or animal fats, but remains uninfluenced by mineral oil.

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