Further studies are necessary to definitely determine the rôle of bacterial products in the causation of death; however, since the loss of plasma-like fluid into the ligated leg was adequate to produce death this would seem to be the most likely explanation.

These findings agree with studies in traumatic shock which show the serious consequences of a decrease of the circulating blood volume as a result of local fluid loss into the tissues.[5, 6]

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Effect of Dinitrophenol, Sodium Citrate, Sodium Bicarbonate, and Citric Acid upon Distribution of Cholesterol.

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The report of Marie[1] that sodium citrate administered by mouth or intravenously reduced the blood cholesterol of rabbits 60% led us to try its effect upon blood cholesterol of other species. It is of interest in this connection to note that dogs with a hyperpyrexia induced by the administration of 10 mg./kg. dinitrophenol showed an increase in blood cholesterol, the initial value of 161 mg. % being elevated to 285 mg. % 2 hours after injection of the drug. These observations led us to continue the study with albino rats.

Five groups of 5 rats each were placed upon a diet similar to that suggested by Chanutin and Ludewig,[2] in which extracted casein was substituted for extracted dried beef. To this cholesterol deficient diet, cholesterol was then added to the extent of 2%. The first group of rats received no supplement and served as control animals. In the second group, each animal received a daily subcutaneous injection of 1 mg. dinitrophenol per 100 gm. body weight. To the third, 0.2 gm. sodium citrate per 100 gm. body weight was given in aqueous solution by stomach tube. The fourth and fifth groups received $NaHCO_3$ and citric acid solutions, respectively, by stomach tube, in order to determine, if possible, the ion responsible for any change in the distribution of cholesterol. These 2 substances were given in amounts furnishing separately the same quantities of

[6] Roome, N. W., Keith, Wm. S., and Phemister, D. B., *S. G. O.*, 1933, **56**, 161.

[1] Marie, A. C., *Compt. rend. Soc. Biol.*, 1932, **109**, 13.

[2] Chanutin, A., and Ludewig, A., *J. Biol. Chem.*, 1933, **102**, 57.

TABLE I.

Series / Range	Control Av.	Control low	Control high	Dinitrophenol Av.	Dinitrophenol low	Dinitrophenol high	Sodium Citrate Av.	Sodium Citrate low	Sodium Citrate high	$NaHCO_3$ Av.	$NaHCO_3$ low	$NaHCO_3$ high	Citric Acid Av.	Citric Acid low	Citric Acid high
Blood mg./100 cc. plasma (Blood of each group pooled for analysis)															
Total chol.	93			108			90			95			77		
Free ''	29			28			23			28			26		
Ester ''	64			80			67			67			51		
Total F. A.	474			431			522			431			284		
Lipoid P	6.07			7.47			6.47			6.17			5.64		
Livers mg./100 gm. body weight															
Total chol.	57	40	63	44	21	50	58	41	65	89	65	101	57	40	61
'' F. A.	247	230	268	198	162	210	265	241	274	357	335	380	240	225	270
Sterols mg./100 gm. body weight															
Carcass	337	326	340	300	285	310	319	305	335	306	285	319	287	251	299
'' + liver	394	383	405	344	320	360	377	360	389	395	380	409	344	321	363
Feces mg./100 gm. body weight (Feces of each group mixed and analyzed as group)															
Sterol	626			773			557			678			633		
Neutral fat	29			37			15			88			84		

sodium and citrate ions as received by the animals in Group 3 on the sodium citrate supplement. Each animal of the fourth group, therefore, received 0.14 gm. $NaHCO_3$, and of the fifth group 0.11 gm. citric acid daily, per 100 gm. body weight. At the end of 3 days the rats were killed, the blood from each group pooled and analyzed for total and free cholesterol, total fatty acids, and lipoid P. The livers were removed and analyzed individually for total cholesterol and total fatty acids, the carcass likewise for total sterols, and the feces for free fatty acids, sterols, and neutral fat. The cholesterol of the blood and liver was determined by means of the Yasuda modification of Okey's method,[3] while for fatty acids Bloor's oxidative method[4] was employed. Lipoid phosphorus was estimated by a modification of the Kuttner-Lichenstein method.[5] The carcass sterols were determined as non-saponifiable material, and the feces were analyzed as described by Gregory and Drummond.[6] The results, calculated on the basis of 100 gm. body weight and averaged for each group, are given in Table I. The range of values obtained by those analyses carried out separately on each animal (*i. e.*, livers and carcass) are also included in the table.

The dinitrophenol increases the cholesterol esters of the blood and reduces the cholesterol of the liver and carcass, while the excretion of sterol is increased. The fatty acids of the blood and liver are reduced slightly. The lipoid P of the plasma is increased.

Sodium citrate has very little effect on the cholesterol of the blood and liver, but reduces the sterol of the feces, and to a slight extent the sterol of the carcass. An increase occurred in the fatty acids of the blood. Our work on the rat is, therefore, not in conformity with the observations of Marie on the rabbit.

$NaHCO_3$ has no effect on blood cholesterol, but increases the sterol of the liver and feces. The carcass sterol is somewhat lowered, but the total sterol (carcass and liver) is unchanged, indicating a shift to the liver. The fatty acids of the blood are reduced, but increased in the liver. Neutral fat excretion is increased.

Citric acid decreases plasma ester cholesterol, fatty acids, and lipoid P. It has no effect on the cholesterol of the liver. The carcass sterol is reduced, but the sterol excretion is unaffected. The neutral fat of the feces is increased. The constancy of free cholesterol of blood is worthy of note.

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[3] Yasuda, M., *J. Biol. Chem.*, 1931, **92**, 303.

[4] Bloor, W. R., *J. Biol. Chem.*, 1928, **77**, 53.

[5] Farmer, C. J., and Winter, I. C., PROC. SOC. EXP. BIOL. AND MED., 1934, **32**, To be published shortly.

[6] Gregory, E., and Drummond, J. C., *Z. für Vitaminforschung*, 1932, **1**, 257.