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Further Rabbit Heart Perfusion Experiments with Amino-Acids.

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We have previously reported[1] our studies on the creatine content of rabbit heart muscle after perfusion of the coronary system with oxygenated Ringer-Locke solution plus glycocoll in a Dawson-Gunn-Locke apparatus. We found that a further modification of the method was necessary in order to maintain the perfusate at a satisfactory pH level. The cause of the greater part of the fall in pH was found to be the CO_2 produced by the heart's metabolism. In order to remove this absorbed and diffusible CO_2, an aerating agitating lift for the perfusate was devised with the use of a suction pump instead of oxygen pressure. The perfusate was then reoxygenated in the reservoir in the constant temperature bath just above the heart cannulae.

It was found that the creatine content of the heart muscle dropped when the pH of the perfusion fluid was allowed to fall below 7.3-7.5 (Table I). When the estimated pH of the fluid in the myocar-

TABLE I.
Influence of pH on Heart Muscle Creatine.

Perfusion Fluid pH	Creatine Mg. %
7.5	166
7.4	156
7.3	152
7.1	146
6.9	139
6.8	130

dial vessels was maintained within these limits, however, failure was postponed for several hours. Eventually there accumulated in the perfusate a non-volatile acid metabolite, lactic acid on the basis of the qualitative test, which caused an agitation-irreversible drop in the pH. In the presence of myocardial infarcts the non-volatile acid metabolites early forced down the pH and lead to a sharp loss in creatine and early failure.

We have previously[1] noted that perfusion of the isolated rabbit heart with Ringer-Locke solution, until it stopped in failure after several hours, resulted in a uniform drop in the creatine content of

[1] Herrmann, G., Decherd, G., and Erhard, P., PROC. SOC. EXP. BIOL. AND MED., 1934, **32**, 547.

the heart muscle. Furthermore, we found that under similar circumstances the addition of glycocoll failed to prevent this creatine loss. This finding has been confirmed in a larger series of hearts perfused under more constant conditions made possible by the modified method described above.

In addition to the glycocoll experiments, we have studied under similarly controlled conditions the effects of several other amino-acids which have been suggested as possible factors in creatine metabolism. Among these we have thus far added to our perfusate arginine, glutamic acid, aspartic acid, methylguanidine, alanine, and creatine itself, with the results shown in Table II. In the same

TABLE II.
Rabbit Heart Muscle Creatine.

Substances used and No. of exp.	Minimum F	Minimum D	Maximum F	Maximum D	Average F	Average D
Controls	143		168		154	
10		652		831		740
Glycocoll	114		155		134	
10		562		730		645
Arginine	100		126		115	
4		462		605		545
Glutamic acid	108		134		116	
4		498		664		581
Aspartic acid	108		148		134	
4		581		682		639
Methylguanidine	126		150		138	
4		598		705		659
Creatine	125		161		138	
9		630		780		689
Alanine	136		205		166	
20		648		896		783
Insulin	111		158		130	
4		492		701		583
Infarcted Hearts	51		99		79	
14		259		531		439

Table I: Values are listed in mg. % of the fresh muscle (F) and of the dried muscle (D). Total creatinine is actually determined, but of this total less than 5 mg. % is preformed creatinine, the remainder being produced by acid hydrolysis of the muscle creatine.

table we have recorded the effects of insulin and of myocardial infarction. Alanine alone of all the substances studied seemed able to maintain and even enrich the creatine content of the heart muscle. Myocardial infarction, regardless of the perfusate used, caused a very sharp fall in the creatine values of the rabbit heart muscle.