Carbon Dioxide Effects on Myocardial Contractility.* (29285)

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There is scant information concerning the *in vitro* myocardial contractile response as influenced by the percentage CO_2 in the aerating mixture. Available evidence indicates that 5% or more of CO_2 was associated with a negative inotropic effect over a period of time(1,2). However, Feigen(3) noted that use of 1% or 5% CO_2 decreased the rate of decline of the developed tension. He concluded that CO_2 had a stabilizing effect on the contractile mechanisms. However, interpretation of the data is complicated by the type of preparation and concomitant variations in both CO_2 and O_2 in his experiments. Therefore, the experiments in this report were designed to determine the effects of 0%, 2%, and 5% CO_2 on the myocardial developed tension with a constant oxygen concentration and with a preparation shown to be adequately oxygenated(4).

Materials and methods. The methods and techniques used were essentially the same as those reported in previous experiments for the rat trabecular preparation(4,5,6). Briefly, the experimental design consisted of 3 groups of eight muscle preparations each. The trabeculae within each group were aerated with either 0%, 2%, or 5% CO_2. Muscles aerated with the gas mixture containing 0% CO_2 actually had approximately 0.03% CO_2 as contributed by atmospheric CO_2. Oxygen content was maintained at 95%. The balance composition consisted of N_2. Muscles were stimulated at 1/sec for a 3-hour period. Records were taken at the times indicated on the Figure. The bathing solution consisted of Ringer's glucose (5 mM) containing leucine, lysine, pyruvate, arginine, and methionine each at 2 mM. The volume of the solution bathing the muscle was 45 ml which was replenished at 8 ml/min. The solution was buffered with 7.1 mM $NaHCO_3$. The pH of the perfusate aerated with either 0%, 2%, or 5% CO_2 was 8.5, 7.5, and 7.2 respectively. The 5% level of significance was used in the statistical analyses.

Results. Fig. 1 is a plot of the mean developed tension of each group of muscles as a function of time. Fluctuations in response were noted during the first 40 minutes in all groups. These variations in developed tension may have been due to alterations in intracellular concentration of either acetylcholine or catecholamines which have been postulated as producing this treppe-type of response(7). Following this there occurred a progressive decline in mean developed tension of those muscles aerated with 5% CO_2. This is the same type of response that Feigen(3) obtained. The mean developed tension of the remaining 2 groups approximately paralleled each other. Paired and group data analyses were performed on the data to determine the stability of the developed tension within a group and to determine also if any significant changes in developed tension occurred between groups, respectively. The results of these analyses are shown in Tables I and II. Muscles aerated with gas mixtures containing 2% CO_2 have a significantly higher developed tension than muscles aerated with 5% CO_2 at the end of a 3-hour period. Also, muscles aerated with 2% CO_2 maintained a consistent developed tension and a small vari-

TABLE I. Paired Data Analysis. Comparison of mean developed tension (mg) within each group at first, second and third hour. A plus or minus sign designates a significant or non-significant difference respectively.

Group*	1st hr vs 2nd hr	2nd hr vs 3rd hr	1st hr vs 3rd hr
2% CO_2 (82, 67, 89)†	—	—	—
5% CO_2 (170, 135, 151)†	+	+	+
0% CO_2 (184, 167, 172)†	+	+	+

* As identified by CO_2 content.
† Values designate standard error of mean at first, second, and third hour, respectively.

* This investigation was supported by PHS grant, Oregon Heart Assn. and Medical Research Foundation.

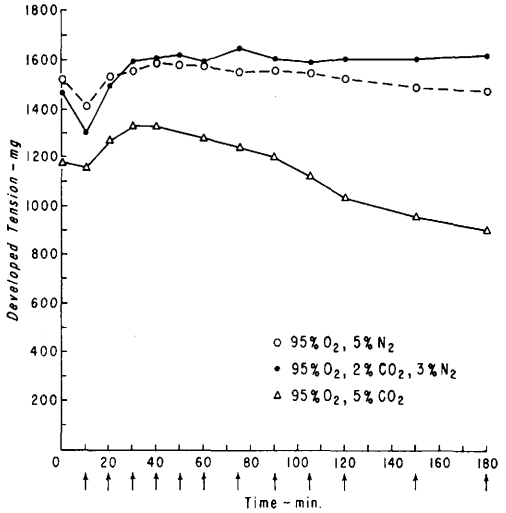

FIG. 1. Mean developed tension of designated groups, plotted as a function of time. Readings were taken at times indicated by arrow. Each point is the mean developed tension of 8 preparations.

ation in response between individual muscle preparations as determined by the small standard error of the mean (Table I). This was not true of the remaining two groups.

Discussion. These results indicate that CO_2 in an aerating mixture affects the myocardial isometric developed tension. The extent that it does influence the contractility is related to the percentage CO_2. The presence of 2% CO_2 in the aerating mixture in contrast to 5% or 0% apparently influences the intracellular environment so as to enable the muscle cells to maintain a consistent level of activity. It appears that virtual absence of CO_2 as opposed to excessive amounts was not conducive to the stability of the myocardial isometric developed tension.

TABLE II. Group Data Analysis. Comparison of mean developed tension between each group at first, second, and third hour. A plus or minus sign designates a significant or non-significant difference, respectively.

Compared group*	1st hr	2nd hr	3rd hr
2% CO_2 vs 5% CO_2	—	+	+
0% CO_2 vs 2% CO_2	—	—	—
5% CO_2 vs 0% CO_2	—	+	+

* As identified by CO_2 content.

Postulated mechanisms of action of CO_2 have been based on alterations in intracellular pH(2), ion movements(8), or in enzyme kinetics(9). Since the influence of CO_2 on the developed tension is not immediately evident, one may infer that the involved mechanism(s) requires a time interval before changes are noted.

Summary. Rat myocardial preparations were stimulated to contract at one per second in an oxygenated Ringer's solution. The effects of 0%, 2% and 5% CO_2 on the magnitude of the isometric developed tension were studied during a 3-hour experimental period. It was noted that muscles aerated with a gas mixture containing 2% CO_2 revealed not only a constant developed tension but also a small variation in contractile response during the experiments. The detrimental effects of the other percentages of CO_2 on the developed tension were not immediately evident.

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Received March 9, 1964. P.S.E.B.M., 1964, v116.