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The Effect of Forced Activity on the LCt50 for Mice Exposed to GB Vapor

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by

Paul Cresthull
William S. Koon
Fred W. Oberst

51980

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Medical Laboratories Research Report No. 68

THE EFFECT OF FORCED ACTIVITY
ON THE LCt50 FOR MICE EXPOSED TO GB VAPOR

by

Paul Cresthull
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July 1951

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Medical Laboratories Research Report No. 68

The Effect of Forced Activity
on the LCt50 for Mice Exposed to GB Vapor

ABSTRACT

OBJECT.

The object of this experiment was to determine the effect of forced activity on the LCt50 for mice exposed 10 minutes to GB vapor.

RESULTS.

The LCt50 with 19/20 confidence limits for mice exposed 10 minutes to GB vapors during forced activity in a rotary cage was 240 (230-250) mg.min./m³ while animals in the same cage but without forced activity gave a value of 310 (290-340) mg.min./m³.

CONCLUSIONS.

Forced activity in mice exposed to GB vapors for 10 minutes lowers the LCt50.

RECOMMENDATIONS.

None.

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Medical Laboratories Research Report No. 68

The Effect of Forced Activity
on the LCt50 for Mice Exposed to GB Vapor

I. INTRODUCTION.

A. Object.

The object of this experiment was to determine the effect of forced activity on the LCt50 for mice exposed 10 minutes to GB vapor.

B. Authority.

Authorized by the Chief Chemical Officer under Project 4-08-02-007, Toxicity of CW Agents Dispersed as Vapors, Test Program No. T22, Cml C Research and Development Program for fiscal year 1950.

II. HISTORICAL.

No information was found in the literature on the toxicity of inhaled GB in animals during forced activity where the respiratory rate is increased. British investigators (1,2) reported that GB dispersed in air is retained to the extent of 95-98% in the respiratory tract. With increasing respiratory rate, as in forced activity one would expect that more GB would enter the body in a unit period of time and yield a lower LCt50 value for any given exposure time. The effect of increased activity on LCt50 was studied on mice placed in a revolving cage to facilitate forced activity.

III. EXPERIMENTAL.

A. Materials and Equipment.

1. Purified GB furnished by the Chemical Division, Chemical Corps Chemical and Radiological Laboratories.

2. 4250 l. constant flow gassing chamber (3).

3. Specially-constructed revolving cage, consisting of a metal and plexiglass drum, 13 inches in diameter and 7 inches wide, mounted on a shaft. The sides were made of plexiglass with numerous holes (over 200) 1/4 inch in diameter for ventilation purposes. The cage was revolved by a motor at 19 rpm, giving a linear velocity of approximately 65 ft./min.

B. Procedure.

Various concentrations of GB dispersed in air by the usual procedure (3) were maintained in the gassing chamber. The airflow in the chamber was approximately 500 l./min. The temperature for all experiments varied between 60° and 82°F., while the relative humidity varied between 28 and 61%. The temperature within the revolving cage (containing 10 mice) was 4°-5° higher after 10 minutes exposure than that within the gassing chamber.

Chamber air samples were collected by drawing a measured volume through two Edgewood collection bubblers arranged in series, each containing 20 ml. of purified tetralin. The absorbed GB was determined by the peroxide-o-dianisidine method (4).

The revolving cage containing the 10 mice was introduced rapidly into the gas chamber containing GB and was exposed for 10 minutes. During the exposure forced activity in the mice was produced by revolving the cage. Controls were run in the same cage without revolving it.

Mortality figures were based on all deaths occurring within a 24 hour period. The LCt_{50} for $t = 10$ min., S the slope function and b the slope were calculated by the method of Wilcoxon and Litchfield (5).

C. Results.

The mortality of mice exposed to various levels of GB vapor under forced activity and under conditions of inactivity is shown in Table 1.

Table 1
Mortality of Mice Exposed to GB Vapor
For 10 Minutes

GB Concentration in Chamber mg./m ³	Number of Animals	Mortality	
		Rotary Cage During Forced Activity %	Rotary Cage During Inactivity %
15	10	-	0
19	10	10	10
23.5	10	20	10
24.5	10	60	20
24.5	10	20	0
25.0	10	80	0
26.0	10	100	50
26.5	10	-	40
32.5	10	-	30
34.5	10	-	70
35.0	10	-	30
39.0	10	-	70
40.5	10	-	80
40.5	10	-	100

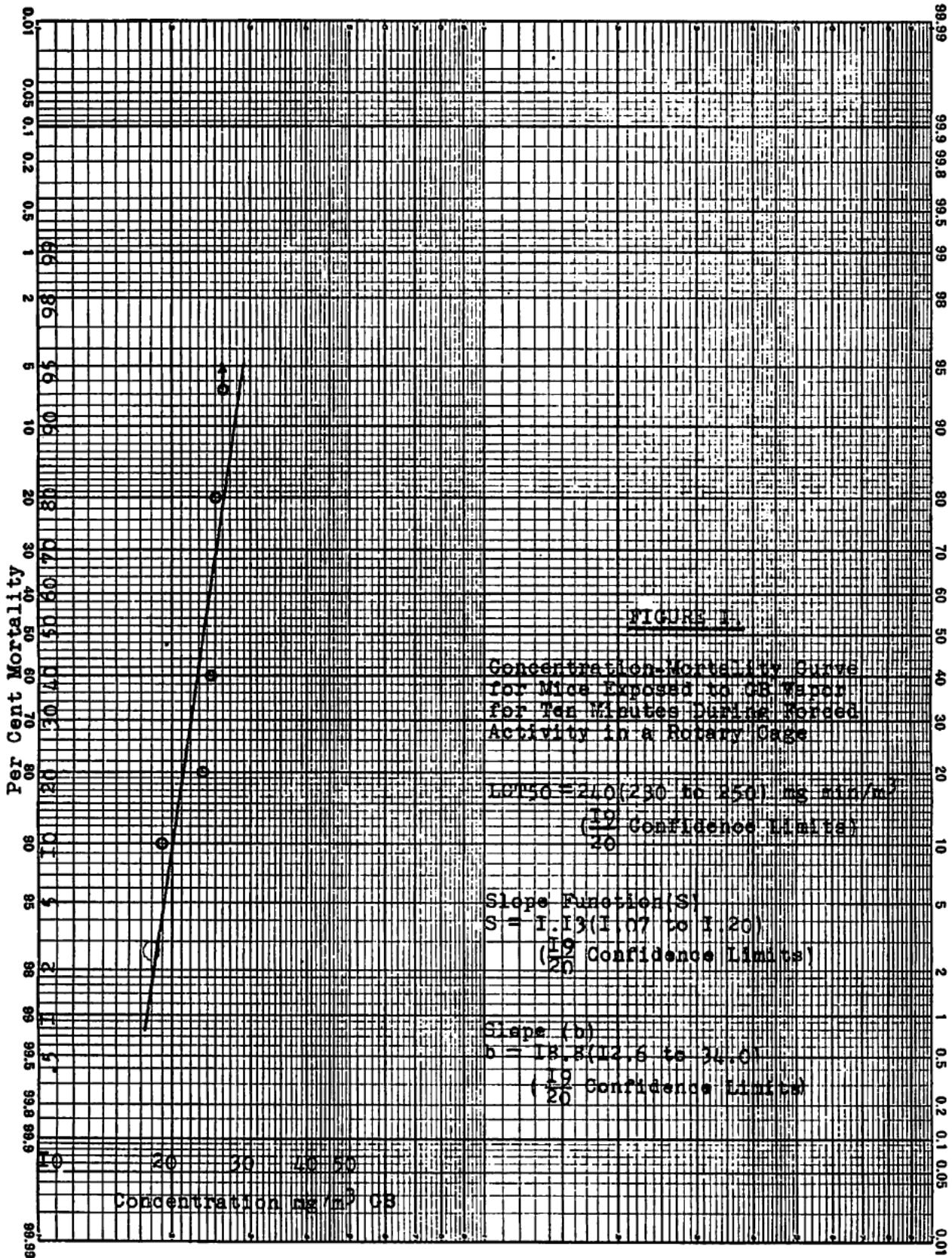
From this table concentration-mortality curves were made as shown in Figs. 1 and 2, in which the mortality for equal concentrations were grouped for the points plotted. The LCt50 with 19/20 confidence limits was calculated for each test. This value for forced activity was 240 mg.min./m³ (230-250) and for the controls with no activity it was 310 mg.min./m³ (290-340). The slope function, S, for the group during activity was 1.13 (1.07-1.20) and during inactivity was 1.37 (1.25-1.51). The slope, b, during activity was 18.8 (12.6-34.0) and during inactivity was 7.3 (5.6-10.3) for confidence limits of 19/20. Since the LCt50 and the slopes for the two tests are significantly different, there is no question that forced activity affects the mortality of mice exposed to GB vapor.

IV. DISCUSSION.

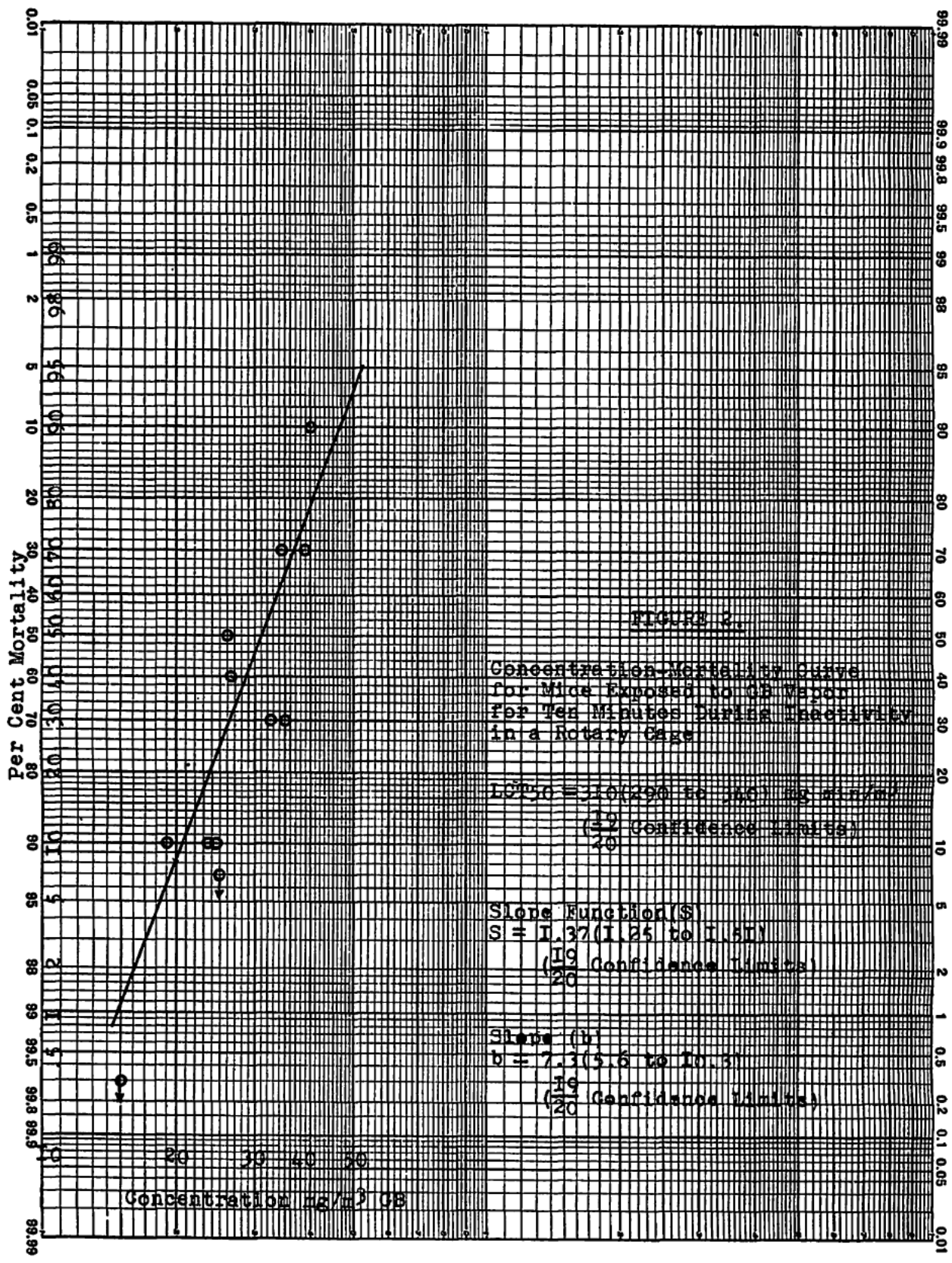
In a previous Medical Division Report (6) it was reported that the LC50 + 1.98 S.E. of GB for mice was 38 + 3 mg./m³, the time of exposure being 10 minutes. The LCt50 is calculated to be 380 mg.min./m³ (350-410). In the present study the controls gave somewhat lower values. The reason for this difference is not apparent. In the earlier report the gassing was carried out in a small 386 l. chamber with an airflow of 250 l./min. In the present study the capacity of the gas chamber was 4250 l. and the airflow was 500 l./min. Temperature and humidity of the air in the rotating chamber and the general health of the mice might possibly be contributing factors to the somewhat greater mortality of the control animals than those in the previous report (6). However, these factors would be the same in the two tests conducted at this time and would not invalidate the conclusions of the study.

It is known that the LCt50 is a function of chamber concentration, consequently, comparisons with other data in the literature must be made for the same exposure time. In all of the tests under consideration the time was 10 minutes. An early British report (7) gave 310 mg.min./m³ for the LCt50 value. More recently (8) they improved their gassing chambers and reported a figure of 342 mg.min./m³ with 5% limits of 316-378. A total of 220 mice were used. The Canadians (9) also working with this agent reported a figure of 240, which is considerably lower than our values or the British. Their figure is in close agreement with those published by the University of Chicago Toxicity Laboratory (10) which is 250 mg.min./m³. The reason for the lack of general agreement is not clear, although the difference in the techniques used may account for some of the discrepancy.

In the present experiments on forced activity where a suitable control was carried along at the same time, there is no question that the LCt50 value was decreased. This is in accord with what might be expected from the British reports (1,2) that approximately 95-98% of GB in inspired air is absorbed. Consequently with increased respiration and minute volume of inspired air, the amount of GB retained in the body is markedly increased. These experiments, however, do not necessarily separate the respiratory effects from the muscular activity associated with forced breathing, although it is believed that the latter plays a minor role in changing the LCt50 value.



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V. CONCLUSIONS.

Forced activity in mice exposed to GB vapors for 10 minutes lowered the LC50, *approximately 20 per cent.*

VI. RECOMMENDATIONS.

None.

VII. BIBLIOGRAPHY.

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The Effect of Forced Activity on the LCt50
for Mice Exposed to GB Vapor

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Authority:

Project No.: 4-08-02-007
Test Program No.: T22

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APPROVAL RECOMMENDED:

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Typed: 9 July 1951
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Colonel, Medical Corps
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