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**BIOCHEMISTRY OF SUBMARINE AND DIVING STRESS:
IV RESPONSES OF BLOOD LACTATE-PYRUVATE AND REDOX STATE
TO CHRONIC EXPOSURE TO 3% CO₂**

by

**Michael J. Jacey, Arthur A. Messier
and Karl E. Schaefer**

**Bureau of Medicine and Surgery, Navy Department
Research Work Unit MF12.524.006-9028BA9K.11**

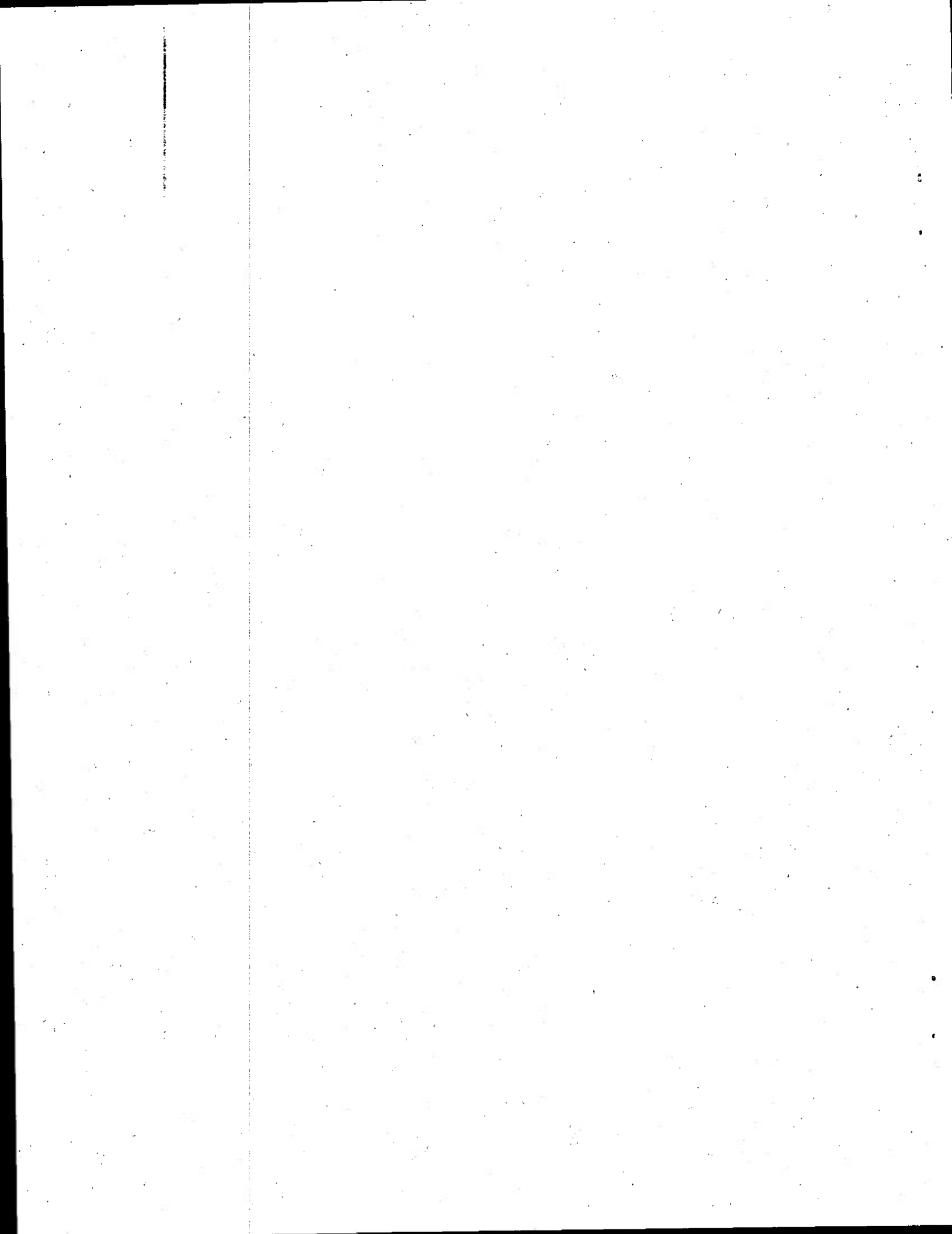
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NAVAL SUBMARINE MEDICAL RESEARCH LABORATORY
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Transmitted by:




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Head, Biochemistry Branch

Reviewed and Approved by:



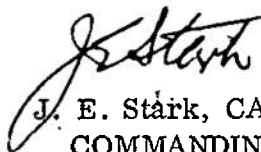
Charles F. Gell, M.D., D.Sc. (Med)
Scientific Director
NavSubMedRschLab

Reviewed and Approved by:



J. D. Bloom, CDR, MC, USN
Officer in Charge
NavSubMedRschLab

Approved and Released by:



J. E. Stark, CAPT, MC, USN
COMMANDING OFFICER
Naval Submarine Medical Center

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SUMMARY PAGE

THE PROBLEM

To investigate and clarify any alterations in blood lactate/pyruvate system and redox state under conditions of acute and chronic exposure to a level of CO₂ that may be potentially encountered in submarine, diving, space, and other closed environments.

FINDINGS

Blood lactate and pyruvate levels as well as redox states were unaffected by acute and chronic exposure to 3% CO₂.

APPLICATIONS

These findings are of interest to cognizant personnel concerned with medical aspects of exposure to CO₂ at levels which may be encountered in submarine, diving, space, and other closed environments.

ADMINISTRATIVE INFORMATION

This investigation was conducted as part of Bureau of Medicine and Surgery Research Work Unit MF12.524.006-9028BA9K -- Time Concentration Exposure Limits of CO₂ in Navy Submarine and Diving Facilities. The present report is No. 11 on this Work Unit. The manuscript was approved for publication on 15 April 1971 and designated as Naval Submarine Medical Research Laboratory Report Number 662.

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ABSTRACT

Lactate and pyruvate concentrations were measured in blood of guinea pigs exposed to 3% CO₂ in 21% O₂, balance N₂ for varying periods of time up to a week. The redox state, NAD⁺/NADH ratio was calculated from the lactate/pyruvate ratio and [H⁺] for each time point. Blood lactate-pyruvate concentrations as well as redox states, were virtually unaffected. It would appear that a respiratory acidosis, induced by exposure to 3% CO₂ with a maximum pH decrease of .12 units, is in itself not sufficient to alter glycolytic metabolism of blood in guinea pigs.

constant, of 6.88×10^{-12} mole/l at 40° . The details and rationale for estimation of the redox state in hypercapnia have been previously described³.

RESULTS

Data on lactate, pyruvate, and lactate/pyruvate ratios of blood in acute and chronic hypercapnia induced by exposure to 3% CO₂ are summarized in Table I. Arterial pH and P_{CO₂} values are displayed in Figure 1. The redox states, NAD⁺/NADH ratios, are shown in Table II.

Blood lactate levels were unaffected by exposure to 3% CO₂. However, pyruvate concentrations tended to increase during the early stages of exposure reaching a significant peak by three days and declined toward control values at seven days. Lactate-pyruvate ratio was not altered during the seven days of hypercapnia. Arterial pH dropped to its lowest value at one hour, rose by six hours, and remained at approximately this level for the rest of the experiment. P_{CO₂} increased to approximately 50 mm Hg at one hour and maintained this level for the duration of hypercapnia. Redox state was unaltered by exposure to this concentration of CO₂.

TABLE I - Responses of Blood Lactate, Pyruvate, and Lactate/Pyruvate Ratio to Prolonged Exposure to 3% CO₂ in 21% O₂, Balance N₂

		Control	1 Hour	6 Hours	1 Day	3 Days	7 Days
Lactate mg %	Mean	20.98	19.52	23.97	24.88	22.44	23.69
	SE	1.47	1.69	2.38	2.20	2.19	1.98
	N	12	10	10	14	14	13
Pyruvate mg %	Mean	.65	.70	.78	.78	.95*	.75
	SE	.08	.09	.04	.12	.08	.10
	N	10	6	6	11	11	9
Lactate/ Pyruvate Ratio	Mean	25.57	28.67	30.90	31.63	23.60	35.24
	SE	5.08	1.60	2.20	4.88	1.11	4.15
	N	9	6	6	11	10	9

* Statistically significant at the 5% level or better.

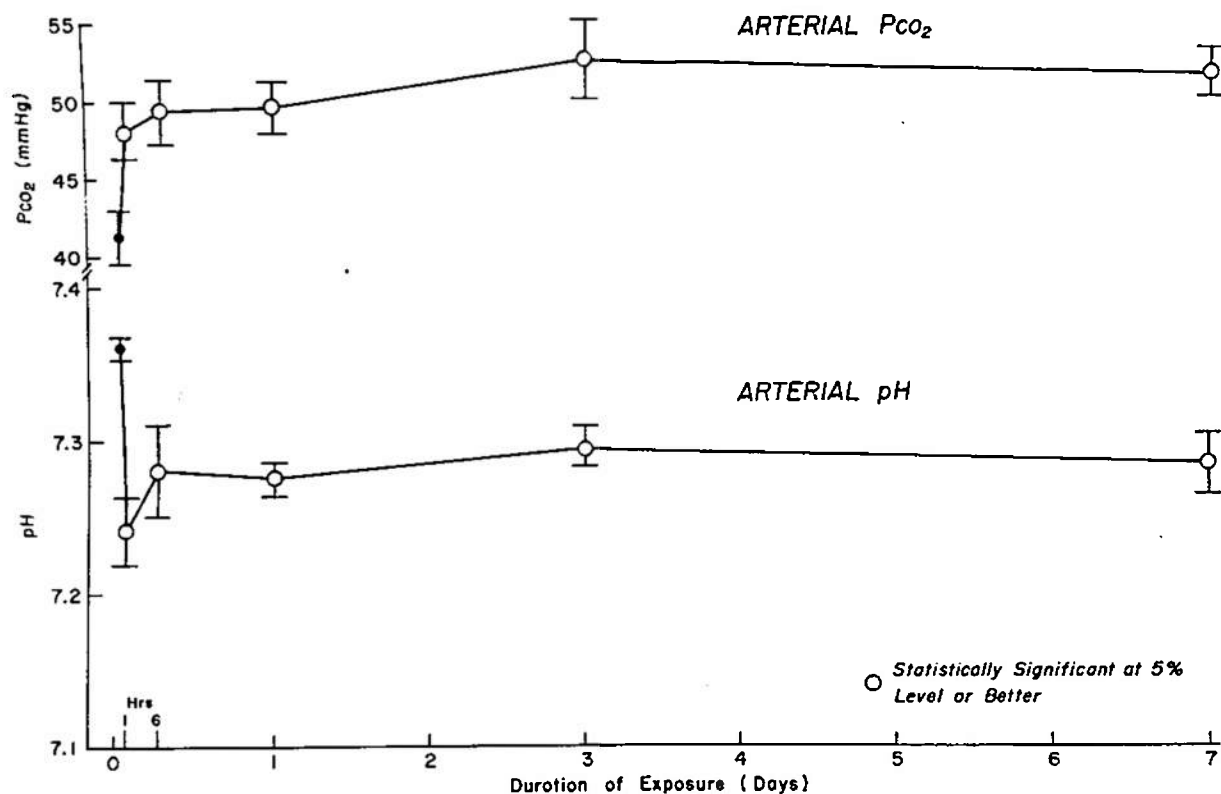


Fig. 1. Effects of chronic exposure to 3% CO₂ on arterial pH and PCO₂.

TABLE II - The Effects of Prolonged Exposure to 3% CO₂ in 21% O₂, Balance N₂ on Blood Redox State, NAD⁺/NADH Ratio

		Control	1 Hour	6 Hours	1 Day	3 Days	7 Days
NAD ⁺ / NADH Ratio	Mean	241.3	296.2	246.4	294.0	328.4	246.9
	SE	37.3	23.0	38.9	34.0	21.2	35.1
	N	9	6	6	11	10	9

DISCUSSION

The decreases in blood lactate and pyruvate content in acute hypercapnia reported by Kazemi et al.⁴ for 10% exposure and by Jacey and Schaefer⁵ for 15% exposure were not seen in the present study. Exposure to 3% CO₂ produced a maximum drop in arterial pH of .12 units and an increase in PCO₂ to approximately 50 mm Hg. Granholm and Siesjö¹¹ studied lactate and pyruvate concentrations in brain and cerebrospinal fluid of cats acutely exposed to a level of CO₂ that produced an arterial PCO₂ of 60 mm Hg and found no important changes in the concentrations of these metabolic acids. Furthermore, in an experiment involving one human subject exposed to progressively increasing levels of CO₂ from 0 to 3% over a period of 15 hours, Schaefer et al.¹¹ detected no alterations in blood lactate and pyruvate content.

Although blood lactate concentration is pH-related, it would appear that an acute respiratory acidosis producing a maximum pH decrease of .12 units is in itself not sufficient to alter glycolytic metabolism of blood. Similarly, it may also be inferred from the data of Murphy⁷ that only slight changes occur in lactate production in erythrocytes by decreasing "in vitro" pH by .1 unit.

The significant increase in pyruvate content without a change in lactate/pyruvate ratio seen at the third day of exposure may have several explanations. Schaefer et al.⁸ have demonstrated that while blood lactate and pyruvate levels may vary widely in humans over a twenty-four hour period, the lactate/pyruvate ratio remained

constant. On the other hand, the increase in pyruvate is reminiscent of the increase of this metabolite which persisted during the early phase of chronic hypercapnia induced by exposure to 15% CO₂³. However, in that case, a decrease in lactate/pyruvate ratio occurred accompanied by an increase in redox state. Changes in pyruvate levels are difficult to interpret by themselves due to the many equilibria that involve pyruvate. The lactate/pyruvate ratio, however, has been shown to be a sensitive indicator of the functional state of cellular metabolism through its relationship to the redox state of the free glycolytic NAD⁺/NADH couplet⁵. Lactate/pyruvate and NAD⁺/NADH ratios were unaffected by the stress of a respiratory acidosis induced by exposure to 3% CO₂.

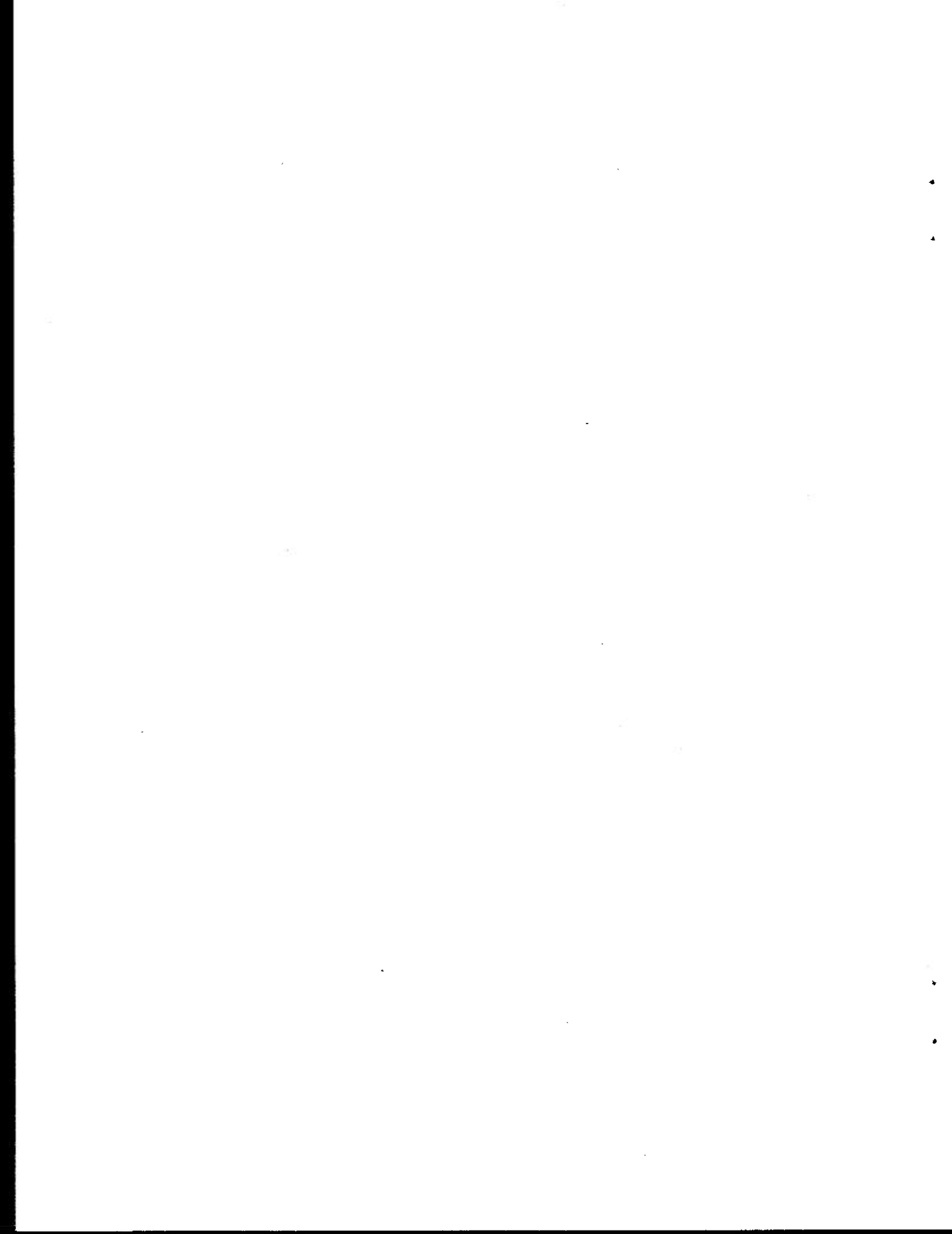
The erythrocyte enzyme, methemoglobin reductase, together with the NAD⁺/NADH pair is responsible for maintaining the iron of hemoglobin in the ferrous state. An increase in redox state might result in an accumulation of erythrocyte methemoglobin. In chronic hypercapnia induced by exposure to 15% CO₂, redox state attained its highest value at one day³. This time point coincided with the peak of methemoglobin content seen under the same experimental conditions by Wood and Schaefer¹². These investigators also found no changes in methemoglobin levels in chronic hypercapnia induced by exposure to 3% CO₂. In the present study no alterations were observed in NAD⁺/NADH ratio under the same exposure conditions.

These results would indicate that the blood glycolytic system in guinea

pigs is not affected by the stress of a respiratory acidosis induced by exposure to this 3% level of CO₂.

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