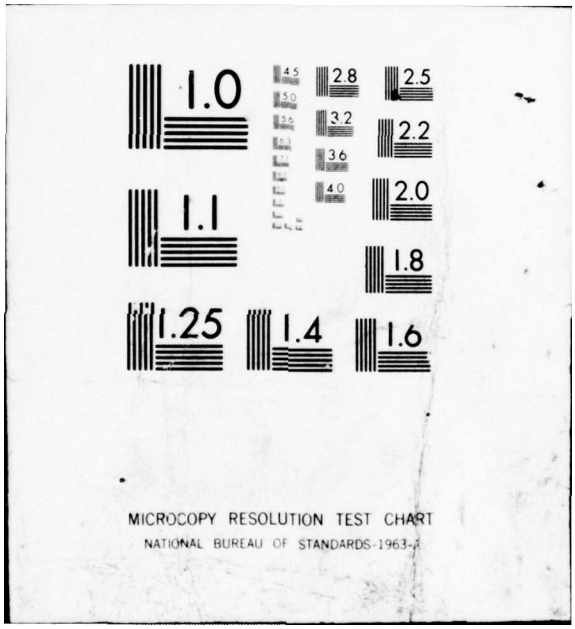
AD-A052 564 ARMY RESEARCH INST OF ENVIRONMENTAL MEDICINE NATICK MASS F/G 6/16
MECHANISMS OF THE CHANGES IN ARTERIAL OXYGEN SATURATION AT ALTI--ETC(U)
FEB 78 J C CRUZ, L H WARTLEY, J A VOGEL

UNCLASSIFIED USARIEM-M-14/78 NL

| OF |
AD
A052564

END
DATE
FILMED
5-78
DDC


1.0
1.1
1.25
1.4
1.6
1.8
2.0
2.2
2.5
2.8
3.2
3.6
4.0
4.5
5.0
MICROCOPY RESOLUTION TEST CHART
NATIONAL BUREAU OF STANDARDS-1963-A

# MECHANISMS OF THE CHANGES IN ARTERIAL OXYGEN SATURATION AT ALTITUDE*

by

Julio C. Cruz,[1]
L. Howard Hartley,[2]
James A. Vogel

16 Feb 78
15 P.

U. S. Army Research Institute of Environmental Medicine
Natick, Massachusetts 01760

USARIEM-M-14/78

16 Feb 78

*Work presented to the Krogh Centenary Symposium, Srinagar, India, October 1974.

[1] On leave from the Instituto de Investigaciones de la Altura, Universidad Peruana Cayetano Heredia, Lima, Peru.

[2] Present address: Department of Medicine, Harvard Medical School, Beth Israel Hospital, Boston, Massachusetts.

The opinions or assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the Department of the Army or the Department of Defense.

This human research study, in protocol form, was reviewed and approved by the Office of The Surgeon General for the Department of the Army in accordance with Army Regulation 70-25.

The ratio of arterial oxygen content to its capacity is called arterial oxygen saturation ($SaO_2$). Its level is dependent on the alveolar gas exchange efficiency. A normal person, breathing room air at sea level, has an average of 97% $SaO_2$. This saturation may fall in a variety of conditions, such as low oxygen breathing or pulmonary disease. It is well known that blood oxygen saturation bears a relationship with the partial pressure of oxygen to which it is exposed. This relationship, known as the oxygen-hemoglobin ($O_2$-Hb) dissociation curve, is also modified by several factors, i.e., pH, temperature.

When a man goes to altitude, the arterial oxygen saturation is modified for many reasons. First, because of the low barometric pressure, the inspired oxygen tension ($P_IO_2$) is low. Therefore the alveolar and the arterial oxygen tension ($PaO_2$) are lower than sea level values. In short, the magnitude of the $SaO_2$ will depend on the $P_IO_2$. Second, once the $PaO_2$ has decreased, the arterial chemoreceptors will be stimulated, therefore the ventilation will be increased. Hyperventilation influences the $SaO_2$ by two mechanisms (fig. 1): a) increasing the $PaO_2$, which will increase $SaO_2$ according to the $O_2$-Hb dissociation curve relationship, and b) producing respiratory alkalosis, which will affect the $O_2$-Hb dissociation curve, shifting it to the left through the pH effect. Average values of $SaO_2$, pH and $PaO_2$ obtained in four sea level subjects (3,10) which sojourned to 4350 m (Cerro de Pasco, $P_B$ 461 torr) are
1 depicted in fig. 1. The circle containing a cross represents two days, and the circle with an X indicates ten days at altitude. On the assumption these subjects would not have hyperventilated, their arterial blood could be predicted to be 32 torr $P_{O_2}$, 62% $S_{O_2}$. Starting from this point, the dotted line shows the increase of $SaO_2$ to 83% due only to increase in $PaO_2$ (constant pH).

The interrupted line labeled alkalosis shows the additional increase in $SaO_2$ to 88% due to the pH effect.

Third. Several investigators have shown that high altitude exposure produces a rightward shift of the $O_2$-Hb dissociation curve (1,6-8). $P_{50}$ (7.4) determinations made on the same subjects (4), are shown in the lower part of fig. 1. Average values were 24 and 28 torr at sea level and high altitude, respectively. The saturation marked on the ordinate should not be considered in this case, since $P_{50}$ by definition is the $P_{O_2}$ pressure at 50% saturation. However, that ordinate gives an idea of the magnitude of the saturation changes that $O_2$-Hb dissociation curve shift will produce in the 24-28 torr range. Although the rightward shift of the $O_2$-Hb dissociation curve at altitude would facilitate the $O_2$ release at tissue level, it is seen in fig. 1 that $P_{50}$ measurements obtained at sea level and at altitude, when calculated to the in vivo (full symbols) pH, have almost the same value. This means that, the shift described in vitro does not have any effect in vivo. Indeed, $SaO_2$ measured was 89% and not 82% that would be obtained were the in vitro phenomenon to take place. Similar conclusion has been reported previously (8).

Once the $SaO_2$ has been reached at altitude in the resting condition, it is further modified when a person performs exercise. Fig. 2 shows the changes in $SaO_2$ observed in the same subjects. Average values obtained in 8 high altitude natives are also included (3,9). This observation, i.e., the fall in $SaO_2$ with exercise at altitude, has been published by several investigators (2,5,11,12). The mechanisms that produce this $SaO_2$ fall are discussed under the remaining three points.

Fourth. Once again, $SaO_2$ will be modified by the ventilation. However the increase in ventilation obtained during exercise is adequate for the metabolic demands, except during heavy work. The final $PaO_2$ obtained during exercise will therefore depend on the alveolar gas efficiency. Our subjects
3 did not modify their $PaO_2$ during heavy work (fig. 3). Thus the $SaO_2$ fall observed, is fully explained by the metabolic acidosis (interrupted line labeled acidosis). However, additional factors are taking place that further change the $SaO_2$.

Fifth. An increase in body temperature occurs during exercise. Assuming a 2°C increase, the calculated saturation would fall to 79% (dotted line of fig. 3) largely because the pH becomes more acid, due to the temperature effect on pH. However at the same time the $P_{O_2}$ rises due to the temperature effect on $P_{O_2}$ (vertical dotted line of fig. 3) and the final calculated saturation is 86%.

Sixth. We have found that during heavy exercise, $P_{50}$ (7.4) shifted to the left (4). Average values are shown in the lowest part of figure 3 at rest (R) and during heavy work (E). The in vivo $P_{50}$ at rest and during exercise are also shown (full symbols). Taking this mechanism into account, i.e., left shift of the $O_2$-Hb dissociation curve, the $SaO_2$ would further rise to 89%.

It is concluded that it appears possible that $SaO_2$ does not change at all in vivo, and what we observe are the in vitro changes due to the acid pH. The same mechanisms in the discussion applies to high altitude native subjects since no differences are observed in $SaO_2$ when compared with sea level subjects (fig. 2).

## Summary

The reasons for the arterial oxygen saturation ($SaO_2$) changes during altitude exposure at rest and during exercise are presented and discussed. $SaO_2$ is prevented to show lower values than usually measured due to hyperventilation. Ventilation increases $SaO_2$ through an elevation of $P_{O_2}$ and pH. No negative contribution is found with the rightward shift of the $O_2$-Hb dissociation curve reported in vitro. The explanation is found on similar $P_{50}$ *in vivo* values shown at sea level and at altitude. The $SaO_2$ fall observed during exercise at altitude is fully explained by the metabolic acidosis (Bohr effect). However, if additional factors are taken into account, such as temperature increase and left shift of the $O_2$-Hb dissociation curve, no changes are expected to occur in vivo.

## REFERENCES


1. Aste-Salazar, H., and A. Hurtado. The affinity of hemoglobin for oxygen at sea level and at high altitude. Am. J. Physiol. 142: 733-743, 1944.
2. Banchero, N., F. Sime, D. Penaloza, J. Cruz, R. Gamboa, and E. Marticorena. Pulmonary pressure, cardiac output and arterial oxygen saturation during exercise at high altitude and at sea level. Circulation 33: 249-262, 1966.
3. Cruz, J.,C., L. H. Hartley, and J. A. Vogel. Effect of altitude relocations upon $AaDO_2$ at rest and during exercise. J. Appl. Physiol. Submitted for publication.
4. Cruz, J. C., L. H. Hartley, and J. A. Vogel. Increase of hemoglobin oxygen affinity during maximal exercise at sea level and high altitude. (Unpublished manuscript).
5. Dempsey, J. A., W. G. Reddan, M. L. Birnbaum, H. V. Forster, J. S. Thoden, R. F. Grover, and J. Rankin. Effects of acute through lifelong hypoxic exposure on exercise pulmonary gas exchange. Respir. Physiol. 13: 62-89, 1971.
6. Keys, A., F. G. Hall, E. S. Barron: The position of the oxygen dissociation curve of human blood at high altitude. Am. J. Physiol. 115: 292-307, 1936.
7. Lenfant, C., P. Ways, C. Aucutt, and J. Cruz. Effect of chronic hypoxic hypoxia on the $O_2$-Hb dissociation curve and respiratory gas transport in man. Respir. Physiol. 7: 7-29, 1969.
8. Torrance, J. D., Lenfant, C., J. Cruz, and E. Marticorena. Oxygen transport mechanisms in residents at high altitude. Respir. Physiol. 11: 1-15, 1970/71.

9. Vogel, J. A., L. H. Hartley, and J. C. Cruz. Cardiac output during exercise in altitude natives at sea level and high altitude. J. Appl. Physiol. 36: 173-176, 1974.

10. Vogel, J. A., L. H. Hartley, J. C. Cruz, and R. P. Hogan. Cardiac output during exercise in sea-level residents at sea level and high altitude. J. Appl. Physiol. 36: 169-172, 1974.

11. Vogel, J. H. K., W. F. Weaver, R. L. Rose, S. G. Blount, Jr. and R. F. Grover. Pulmonary hypertension on exertion in normal man living at 10,150 feet (Leadville, Colorado). Med. Thorac. 19: 461-477, 1962.

12. West, J. B., M. B. Gill, S. Lahiri, J. S. Milledge, L. G. C. E. Pugh, and M. P. Ward. Arterial oxygen saturation during exercise at high altitude. J. Appl. Physiol. 17: 617-621, 1962.

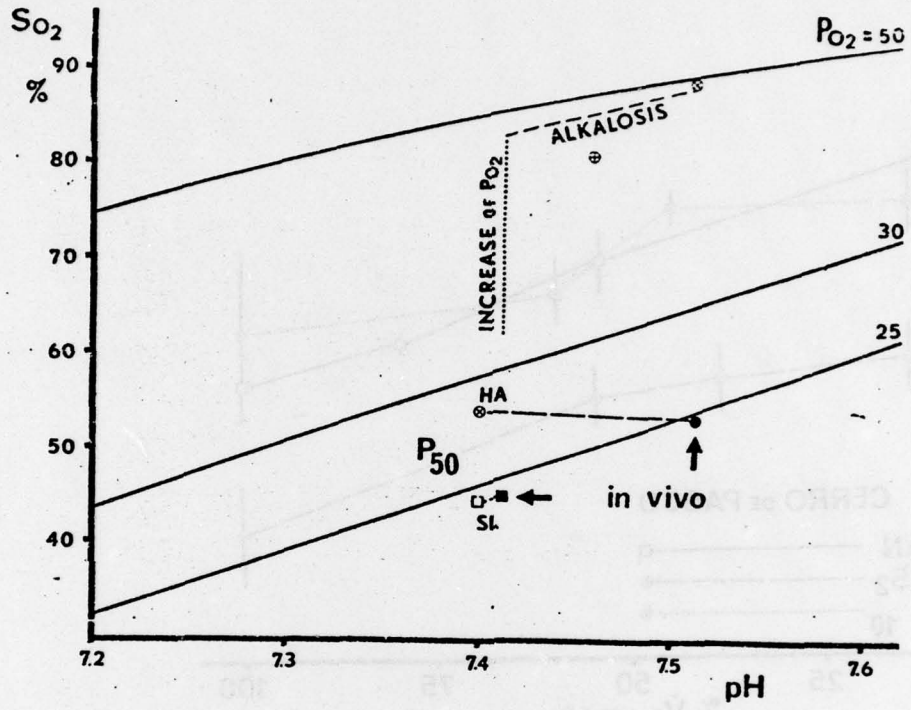
FIGURE LEGENDS

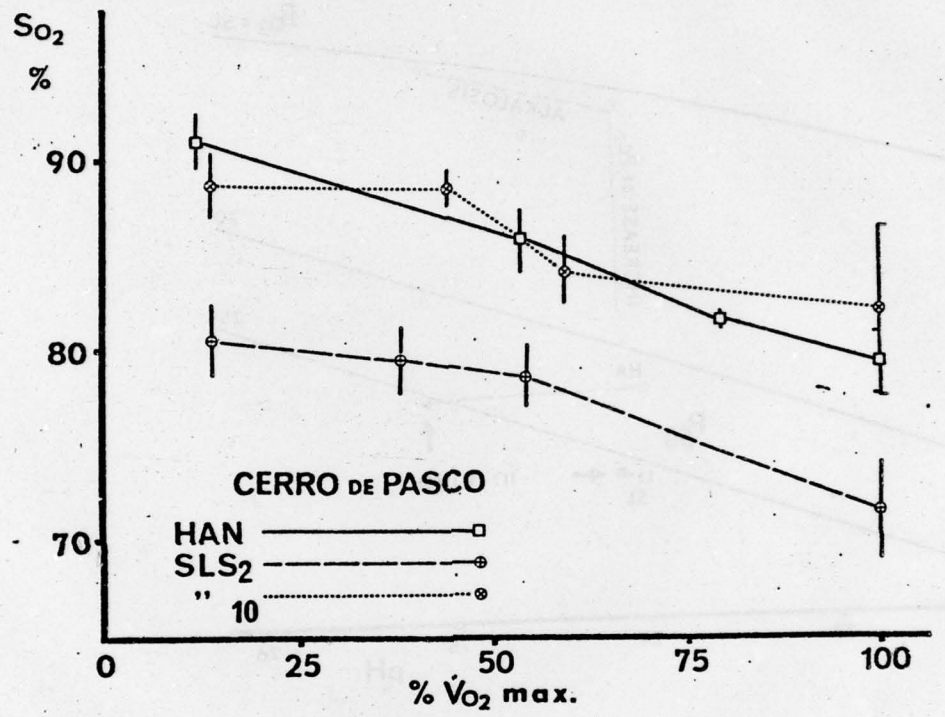
Fig. 1 Arterial oxygen saturation ($SaO_2$) changes due to altitude exposure in resting conditions. Mean values of $SaO_2$, pH and $PaO_2$ obtained in four sea level subjects sojourning at 4350 m are plotted on a saturation-pH diagram. Circle with a cross: 2nd day, and circle with an X: 10th day at altitude. Three iso-$PO_2$ lines are also drawn. The changes in $SaO_2$ due to hyperventilation (62 to 88%) are represented a) by an increase of $PO_2$ at a constant pH (dotted line) and b) by the resultant alkalosis at a constant $PO_2$ (dashed line). Mean $P_{50}$ values obtained at sea level (SL, circles) and at altitude (HA, squares) are also shown. Saturation scale should not be considered in this case. The calculated in vivo $P_{50}$'s (full symbols) show similar values at SL and at HA, which explain the lack of effect of the rightward shift of the $O_2$-Hb dissociation curve on $SaO_2$.

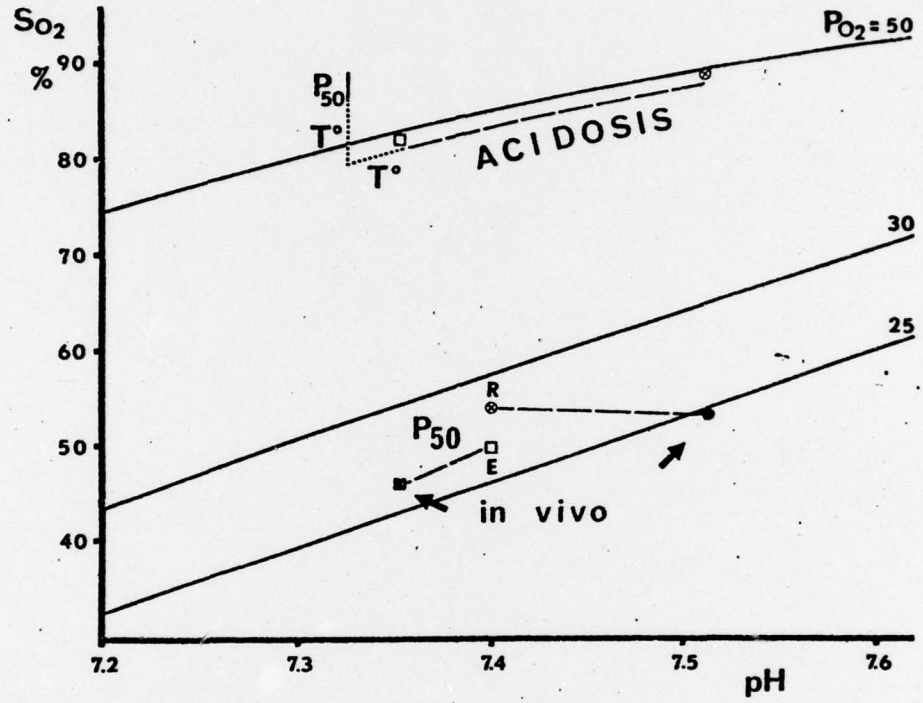
Fig. 2 Mean $\pm$ SE of arterial oxygen saturation ($SaO_2$) as a function of relative oxygen uptake obtained at high altitude, 4350 m (9,10). Note the low $SaO_2$ values obtained at the 2nd day at altitude (dashed line) of sea level subjects (SLS) and their increase at the 10th day (dotted line) reaching similar values to high altitude natives (HAN, continuous line).

Fig. 3 Arterial oxygen saturation ($SaO_2$) changes obtained with heavy exercise at altitude. Similar diagram to figure 1. Symbols are mean values obtained at rest (R, circles) and during maximum oxygen uptake (E, squares) in four sea level subjects after 10 days at altitude. The arterial oxygen saturation ($SaO_2$) change observed is fully explained by the pH shift due to

metabolic acidosis (dashed line labeled acidosis). However, if we take into account the effect of temperature effect on pH and $PO_2$ (dotted line) and the left shift of $P_{50}$, 7.4 (continuous line), the final $SaO_2$ is similar to the resting value, which suggests the possibility that no changes in $SaO_2$ are taking place in vivo. Mean $P_{50}$ values shown in the lower part of the figure as discussed in fig. 1.


$S_{O_2}$
%
90
80
70
60
50
40
$P_{O_2}$ = 50
ALKALOSIS
INCREASE of $P_{O_2}$
30
25
HA
$P_{50}$
in vivo
St.
7.2
7.3
7.4
7.5
7.6
pH


$S_{O_2}$
%
90
80
70
CERRO DE PASCO
HAN
$SLS_2$
" 10
0
25
50
75
100
% $\dot{V}_{O_2}$ max.


$S_{O_2}$
%
90
80
70
60
50
40
$P_{O_2}$=50
$P_{50}$
T°
T°
ACIDOSIS
30
25
R
$P_{50}$
E
in vivo
7.2
7.3
7.4
7.5
7.6
pH

UNCLASSIFIED

SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

| REPORT DOCUMENTATION PAGE | | READ INSTRUCTIONS BEFORE COMPLETING FORM |
|---|---|---|
| 1. REPORT NUMBER<br>M 14/78 | 2. GOVT ACCESSION NO. | 3. RECIPIENT'S CATALOG NUMBER |
| 4. TITLE (and Subtitle)<br>Mechanisms of the Changes in Arterial Oxygen Saturation at Altitude. | | 5. TYPE OF REPORT & PERIOD COVERED<br>6. PERFORMING ORG. REPORT NUMBER |
| 7. AUTHOR(s)<br>Julio C. Cruz, L. Howard Hartley and James A. Vogel | | 8. CONTRACT OR GRANT NUMBER(s) |
| 9. PERFORMING ORGANIZATION NAME AND ADDRESS<br>USA Research Institute of Environmental Medicine, Natick, MA 01760 | | 10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS |
| 11. CONTROLLING OFFICE NAME AND ADDRESS<br>USA Medical Research and Development Commander Washington, DC 20314 | | 12. REPORT DATE<br>16 Feb 78<br>13. NUMBER OF PAGES<br>13 |
| 14. MONITORING AGENCY NAME & ADDRESS(if different from Controlling Office) | | 15. SECURITY CLASS. (of this report)<br>15a. DECLASSIFICATION/DOWNGRADING SCHEDULE |

16. DISTRIBUTION STATEMENT (of this Report)

Distribution of this document is unlimited.

DISTRIBUTION STATEMENT A
Approved for public release; Distribution Unlimited

17. DISTRIBUTION STATEMENT (of the abstract entered in Block 20, if different from Report)

NA

18. SUPPLEMENTARY NOTES

To be published in Proceedings of the Krogh Centenary Symposium.

19. KEY WORDS (Continue on reverse side if necessary and identify by block number)

oxygen-hemoglobin ($O_2$-Hb)

P sub $O_2$

20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

The reasons for the arterial oxygen saturation ($SaO_2$) changes during altitude exposure at rest and during exercise are presented and discussed. $SaO_2$ is prevented to show lower values than usually measured due to hyperventilation. Ventilation increases $SaO_2$ through an elevation of $P_{O_2}$ and pH. No negative contribution is found with the rightward shift of the $O_2$-Hb dissociation curve reported in vitro. The explanation is found on similar $P_{50}$ in vivo values shown at sea level and at altitude. The $SaO_2$ fall observed during exercise at (cont next pg)

P sub 50

DD FORM 1 JAN 73 1473 EDITION OF 1 NOV 65 IS OBSOLETE

SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

(cont from previous pg)

20. cont'd

altitude is fully explained by the metabolic acidosis (Bohr effect). However, if additional factors are taken into account, such as temperature increase and left shift of the $O_2$-Hb dissociation curve, no changes are expected to occur in vivo.