7. Sherry, S., Troll, W., and Wachman, J., *J. Biol. Chem.*, 1954, v208, 85.

8. Seegers, W. H., and Alkjaersig, N., *Arch. Biochem. and Biophysics*, 1956, v61, 1.

9. Seegers, W. H., and Smith, H. P., *Am. J. Physiol.*, 1942, v137, 348.

10. Monkhouse, F. C., France, E. S., and Seegers, W. H., *Circulation Research*, 1955, v3, 397.

11. Seegers, W. H., *Advances in Enzymology*, 1955, v16, 23.

Received February 8, 1957. P.S.E.B.M. 1957, v94.

Effect of Environmental Oxygen Tension on Intestinal Iron Absorption.* (23061)

DONN L. SMITH, MAX E. BIERWAGEN AND THOMAS K. EARLY

Department of Pharmacology, University of Colorado School of Medicine.

Recent reports by Reismann *et al.*(1) indicate that dissociable iron salts are readily absorbed through anatomically intact intestinal mucosa. Although the actual amount absorbed is small, toxic and lethal effects may result. Numerous studies have shown that intestinal absorption of iron is influenced by various types of anemia and fever(2). Granick(2) has postulated that oxygen content of the intestinal mucosal cells may influence absorption of iron by modification of the redox potential within the cell.

The purpose of this investigation was to study the relative amounts of ferrous iron absorbed at widely divergent oxygen tensions in the environmental air. It was desired to determine the effects of oxygen tension without accompanying anemia, infection, or modification of the diet.

Methods. Male and female albino rats, ranging in size from 150 g to 250 g were employed as test animals. All animals were starved for 24 hours prior to experimentation. Iron was administered in dose of 100 mg/kg of elemental iron as ferrous sulfate by stomach tube. Control serum iron levels were determined for each animal, following which the animals were fed the iron and immediately exposed to environmental oxygen tensions of 3 widely varying amounts. One group was exposed to oxygen tension of 54 mm Hg obtained by placing the animals at a simulated altitude of 26,000 feet. A second group remained at ambient oxygen pressure of 125 mm Hg (Denver altitude, 5,280 feet). A third group was exposed to pure oxygen at total pressure of 1390 mm Hg. The oxygen tensions and values employed are approximate, varying slightly with day to day barometric pressure and temperature. After 2 hours exposure to various oxygen tensions, the total serum iron was again determined. All serum iron values were obtained by modification of spectrophotometric method of Barkan and Walker(3) in which o-phenanthroline is used. Blood samples of 1.5 cc were drawn under light ether anesthesia from the right external jugular vein for serum iron determinations. A large number of control serum iron levels were made. One control group was exposed to 54 mm Hg oxygen and a second control group was placed in 1390 mm Hg oxygen for 2 hours without administration of iron. There was no visible necrosis or significant inflammation noted in the intestinal tract of animals autopsied at end of experimental periods.

Results. The results are tabulated in Table I. There was a significant increase in total serum iron levels in all 3 iron-fed groups. In addition there was a significant difference between serum iron values for each group of animals at each oxygen tension level. There was a small difference from control levels in animals exposed to high or low oxygen tensions, but not administered iron. A large group of control serum iron values were determined to establish the normal levels for the rat colony, including sex differences.

Discussion. From the observed results it

* This investigation was supported in part by Natl. Heart Inst. Grant. N.I.H.

TABLE I. Total Serum Iron Levels at Low, Ambient and High Oxygen Tension.

Groups	No. animals	Total serum iron, μg % Normal	2 hr after varied O_2 tensions	% incr. over own controls	C.R.	C.R.*
Controls	85	182 ± 6‡				
Fe + low O_2 tension	15	210 ± 15	454 ± 38‡	+116	5.9	7.4 *
" + ambient "	17	177 ± 16	327 ± 24	+ 84.8	3.0	3.3 *
" + high "	16	158 ± 11	225 ± 19	+ 42.4	5.2	
No Fe, low O_2 tension	13		207 ± 30			.81†
" " high "	10		139 ± 33			1.28†

* C.R. $= \frac{D}{\alpha \text{ diff.}}$, compared to Fe + high O_2 tension. † Compared to normal controls.

‡ Stand. error.

appears that environmental oxygen tension does affect relative rate of ferrous iron absorption from the gastro-intestinal tract. Inasmuch as the non-beta-globulin bound iron is believed to leave the circulation rapidly(4), the serum iron level may not provide an accurate measurement of amount of iron absorbed. However, due to the short experimental period (2 hours) and the very small amount of iron absorbed at the dose level employed(1), it is felt that a reasonable estimation of relative rates of absorption was obtained. The effect of widely varied environmental oxygen tensions, as measured by serum iron levels, was rapid, being manifested within 2 hours. The mechanism by which low or high oxygen tension modifies iron absorption from the gastro-intestinal tract is unknown. Changes in liver and spleen iron content are known to occur at high altitudes (5). Hypoxia has been shown to increase succinic dehydrogenase levels(6). These phenomena are probably too slow in onset to explain the results of our experiments. Granick(2) hypothesizes that oxygen tension at the intestinal mucosal cell may affect passage of iron through the cell by modifying the redox potential within the cell. Low oxygen tension may retard oxidation of ferrous iron to ferric iron, and facilitate reduction of ferric iron to ferrous iron. Conversely, high oxygen tension could increase oxidation of ferrous iron to ferric iron. Such changes in oxidation-reduction potential within the mucosal cell, if they do occur, offer a possible explanation for increased iron absorption in presence of hypoxia, and a relative decrease in absorption during hyperoxia. The results obtained in these experiments indicate that iron absorption from the gastro-intestinal tract is a dynamic cellular process, and not a matter of simple diffusion.

Summary. 1. The effects of exposure of albino rats to 2 hours of low, high and ambient environmental oxygen tensions upon intestinal iron absorption were studied. 2. Total serum irons were increased 116%, 84.8% and 42.4% at environmental oxygen tensions of approximately 54, 125, and 1390 mm Hg respectively.

1. Reismann, K. R., Coleman, T. J., Budac, B. S., and Moriarty, L. B., *Blood,* 1955, vX, 35.

2. Granick, S., *Bull. N. Y. Acad. Med.,* 1954, v30, 81

3. Barkan, G., and Walker, B. S., *J. Biol. Chem.,* 1940, v135, 37.

4. Flexner, L. B., Vosburgh, G. J., and Cowie, D. B., *Am. J. Physiol.,* 1948, v153, 503.

5. Keller, J. G., *ibid.,* 1955, v183, 633.

6. Criscuolo, D., Clark, R. T., and Mefford, R. B., *ibid.,* 1955, v180, 215.

Received February 11, 1957. P.S.E.B.M., 1957, v94.