same point [see 9(a)]. Furthermore the drop in the lactic acid level was obtained when patients with true polycythemia were submitted to more strenuous exercise. Thus, as indicated in Table V, when patients 3, 7 and 9 were submitted to increased work 3(a), 7(a), and 9(a), the same response was still obtained. From these observations we can conclude that the hemoglobin and red blood count level is not the factor which is responsible for the decrease in the blood lactate level in true polycythemia, inasmuch as the response is still obtained at lower ranges.

It is believed that these observations indicate that at rest, the blood flow, particularly through the muscles and perhaps certain glands producing lactic acid, is diminished below normal levels, and that anaerobic metabolic processes lead to the accumulation of abnormal amounts of lactic acid in the blood. With mild exercise the blood flow through muscle is greatly increased and the oxygen supply raised enough to prevent the lactate production. This view is supported by the additional observation that a polycythemic patient responded to a hot bath of 15 minutes' duration by a decrease in blood lactic acid. The fact that the same response occurs in the polycythemia rubra vera patient after reduction of the red cell count to normal, as when the count was elevated, indicates that the disturbance in lactate metabolism is dependent upon some primary factor such as a vasoconstriction, to which the polycythemia is itself secondary. These results seem to indicate, therefore, that tissue anoxia may be an important link in the chain of pathological processes involved in polycythemia vera, and that the primary disturbance may be a persistent vasoconstriction in certain tissues.

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Artificially Produced Anoxia as a Means of Demonstrating Abnormal Respiratory Function.

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A considerable degree of pulmonary collapse can be maintained in man with very little alteration of respiratory function other than an abnormal amount of hyperventilation on exertion. Latent physio-

logical abnormalities usually become manifest clinically only under stress. The response to exercise is too dependent upon physical fitness to be a reliable guide to the capacity of an individual to compensate for a reduction of lung volume. Since oxygen lack constitutes the greatest danger to patients who have disorders of respiration, the oxygen saturation of the arterial blood while breathing a mixture of gases containing less oxygen than the atmosphere would seem to furnish a simple and quantitative test of one phase of respiratory efficiency while the subject remains at rest.

The procedure consists in the analysis of the alveolar air and arterial blood while the subject breathes room air and again while he breathes from a Douglas bag containing about 16% oxygen in nitrogen. By this means it is possible to ascertain the degree of arterial saturation produced by the observed alveolar oxygen tension. Alveolar air was withdrawn in 1 or 2 cc portions from the axial stream in the center of the mouthpiece of a set of respiration valves at the end of successive expirations until 40 cc or more were obtained. This is essentially a modification of the method of Krogh and Lindhard[1] which was shown by Debenham and Poulton[2] to give results which agree with Haldane-Priestley samples. Air analyses were done in the Haldane-Henderson apparatus.

Arterial puncture is often painful and frequently causes patients to hold their breath or hyperventilate, and full reliance cannot always be placed upon the analysis of blood obtained by this means.[3] Since 2 samples of blood are taken within a few minutes of each other in this procedure, the method of Goldschmidt and Light[3] was used. In this method the forearm is immersed in water at 45-47°C for 10 minutes and blood is drawn with gentle suction from one of the veins on the dorsum of the hand. Since the tissues from which it comes are relatively low in metabolism and the vessels are sufficiently superficial to allow the heat to be effective in dilating most, if not all of them, the blood obtained is, as far as gas content is concerned, indistinguishable from that taken directly from an artery. Repeated sampling at one time is also possible. Blood gas analyses were done in the manometric apparatus of Van Slyke and Neill.

The average values for the observed saturation, the calculated saturation, and the difference between the two while the subjects breathed room air and 16% oxygen in nitrogen respectively, are given in Table I. For convenience in analysis, the 52 patients with

1 Krogh, A., and Lindhard, J., *J. Physiol.*, 1913-14, **47**, 431.

2 Debenham, L. S., and Poulton, E. P., *Quart. J. Med.*, 1918-19, **12**, 38.

3 Goldschmidt, S., and Light, A. B., *J. Biol. Chem.*, 1925, **64**, 53.

TABLE I.

Difference Between Observed and Calculated Arterial O_2 Saturation at Observed Alveolar O_2 Tension with Subject Breathing Room Air and 16% O_2 Respectively.

		Room Air				16% Oxygen				
			Arterial O_2 saturation, %				Arterial O_2 saturation, %			
Group	No. of cases	Alv. O_2 tension mm Hg	Observed	Calculated	Dif. D_1	Alv. O_2 tension, mm Hg	Observed	Calculated	Dif. D_2	D_2-D_1
Normals	10	103.6 (96.1-111.9)	98.1 (96.3-99.3)	98.8	0.7	69.3 (61.4-79.2)	93.1 (89.4-96.4)	93.8	0.7	0.0
I	18	105.2 (98.2-117.0)	97.7 (95.8-99.3)	98.9	1.2	74.8 (68.4-83.8)	91.6 (90.0-93.0)	95.1	3.5	2.3
II	18	103.7 (89.1-112.1)	97.0 (94.3-98.8)	98.8	1.8	73.0 (64.2-83.6)	87.7 (85.2-89.6)	94.6	6.9	5.1
III	16	102.0 (89.6-110.8)	93.9 (87.0-98.0)	98.7	4.8	71.3 (64.6-78.4)	80.8 (56.7-84.9)	94.3	13.5	8.7

The figures in parentheses represent the extreme range of variation.

pulmonary disease (of whom 42 had various forms of unilateral and bilateral pulmonary collapse, 6 had tuberculosis without collapse and 4 had silico-tuberculosis without collapse) are divided into 3 groups on the basis of their ability to saturate their arterial blood while breathing the low-oxygen mixture: Group I (18 patients), above 90%; Group II (18 patients), between 85% and 90%; and Group III (16 patients), below 85%. The factors D_1 and D_2 represent in each case the difference between the experimentally determined arterial saturation and the saturation which should exist at its respective alveolar oxygen tension (calculated from an oxygen dissociation curve). The fact that the average values for the normal group (15 determinations on 10 subjects) fall within 0.7% of the curve establishes the validity of these methods of sampling and analysis.

It will be noted that there is a progressive increase in the values of both D_1 and D_2, indicating a failure on the part of the abnormal subjects to attain a degree of saturation commensurate with the alveolar oxygen tension. It will also be noted that this failure to maintain a normal oxygen tension in the arterial blood is strikingly magnified by breathing 16% oxygen in nitrogen. It would seem, therefore, that functional abnormalities which are not apparent under normal conditions can be brought to light by a respiratory strain without the complicating factor of lactic acid production and oxygen debt resulting from exercise. The discrepancy between actual arterial saturation and the saturation which should obtain at the existing alveolar oxygen tension suggests that the diffusion of oxygen through the pulmonary epithelium is retarded in the presence of disease and, to a much lesser extent, collapse of one or both lungs. Whether this is due to a change in the membranes themselves or to an alteration in the ratio between circulation and ventilation, either local or general, is now under investigation.