potent material, she showed no signs of relapse and her erythrocyte count was 5.1 million and hemoglobin 103%.

The fourth patient was also in remission. Her erythrocyte count was 4.8 million and hemoglobin 100%. She was given only a relatively large dose or the equivalent of 265 gm. of liver in one intramuscular injection of extract. After 56 days, she had begun to show mild signs of relapse as evidenced by slight gastro-intestinal symptoms; but the erythrocyte count and hemoglobin level showed very little change.

From these 4 cases, we cannot conclude that all patients with pernicious anemia would be able to store the excess of massive doses of active principle given over a short period of time. Nor can we say that any one of these patients was able to store a calculated amount of the material, because so far the remission of none of them has been as long as if the massive dose were given as small doses over a period of 20 or 30 weeks. However, each of these patients shows evidence of storage of some of the active principle, which storage has enabled each one to maintain normal blood levels for a relatively long period of time.

8460 C

Partial Pressure of Oxygen in Arterial Blood of Patients: Description of an Aerotonometer Method.

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The partial pressure of oxygen in the arterial blood has been measured indirectly by interpolation of O_2 content on the oxyhemoglobin dissociation curve, and by estimation of solubilities of CO and O_2 in the subject's blood (Haldane), and directly by aerotonometry. The latter method has been used by Krogh[1] and by Barcroft and Nagahashi.[2] In this method of the latter authors some difficulty is experienced in keeping the equilibration pressure constant and in securing repeated samples of the small gas bubble for analysis. The present method avoids these two difficulties.

It has been customary to study anoxemic patients by determining the oxygen saturation of the arterial blood and to assume that the

[1] Krogh, A., and Krogh, M., *Skand. Arch. Physiol.*, 1910, **23**, 179.

[2] Barcroft, J., and Nagahashi, M., *J. Physiol.*, 1921, **55**, 339.

oxyhemoglobin dissociation curve is shifted only as changes in the pH take place. Barcroft[3] has studied the partial pressure of oxygen in a few such cases. However, it seemed that a simple, direct method for measurement of oxygen tension would permit a more exhaustive exploration of this field.

About 20 mil. of blood is drawn under anaerobic conditions from a femoral artery into an oiled syringe containing a bit of oxalate-fluoride and mercury, which facilitates mixing. About 10 mil. is then injected into the tonometer chamber in which 0.1 cc. of alveolar air has been placed by sticking the needle through the rubber tube (Fig. 1). The blood foams and mixture is easy with shaking. The

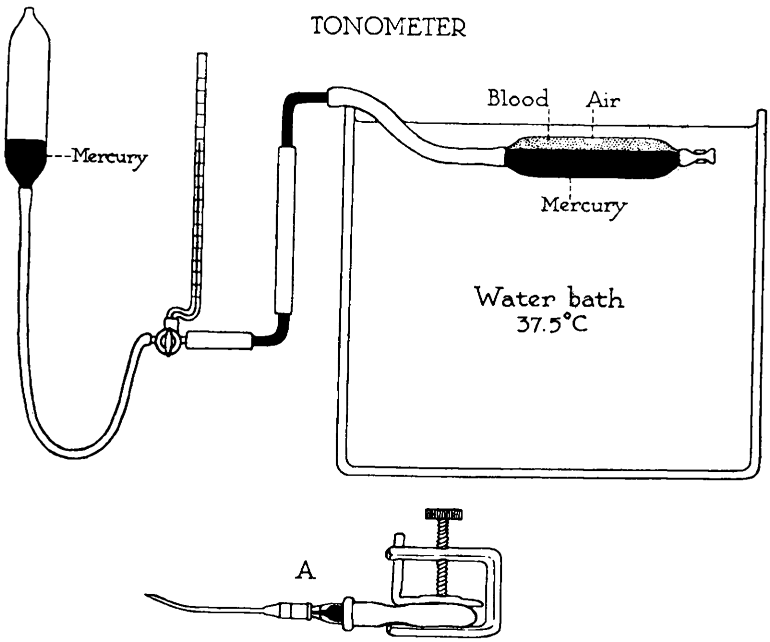

Fig. 1.
The tonometer chamber with its reservoir is connected with a capillary manometer tube. The sampling device is shown below.

remaining blood has its oxygen content and capacity determined in duplicate by standard methods on the Van Slyke manometric gas analysis apparatus.

Samples of the foam are withdrawn after about 10 minutes' shaking at 37.5°C. For this purpose the screw adjusted pipette shown in Fig. 1A is used. The pipette consists of a curved needle with adapter fitted into the bulb of an ordinary medicine dropper and adjusted by a screw clamp. A drop of octyl alcohol is used to

[3] Barcroft, J., *Resp. Function of the Blood*, Cambridge, 1914, pp. 226, 282.

moisten the rubber before the whole device is filled with mercury. The tonometer bulb is kept under a known positive pressure of from 10 to 40 mm. by the adjustment of the mercury reservoir. Since the equilibration system is under a positive pressure the pinch cock can be opened for an instant, and while a little blood escapes into the bath, the needle can be inserted to reach the foam. The small samples consisting of about 20 mm. are analyzed serially in the familiar micro-analysis device of Krogh, using air-free normal salt solution or air-free water for filling the burette.

One correction must be made on the analytical results for CO_2 loss in handling the small bubble. It is assumed the arterial blood carries CO_2 at the partial pressure at which that gas is found in the alveolar air. Hence the small bubble should have the same CO_2 content as the patient's alveolar air. The correction is as follows: The observed O_2 content of the small bubble in percent is multiplied by 100% less the difference in the alveolar CO_2 and observed CO_2 percentages.

A small calculation for the whole method is as follows:

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Trial	Micro burette reading	Change in length with absorption	% of Gas	Alveolar CO_2 %	Corrected O_2 content
	mm.	mm.			%
I.	96.1				
	92.0	CO_2 4.1	4.27	5.37	
	81.3	O_2 10.7	11.14		11.0
II.	59.0				
	56.5	CO_2 2.5	4.27	5.37	
	50.0	O_2 6.5	11.02		10.9
				Mean	10.9(5)

Partial pressure O_2 = 10.9(5) % (B + p — W) = 81.2 mm.
B = 745 mm., p = +40 mm., and W = 43 mm.
(p is the positive pressure in the tonometer system. W is the vapor pressure of normal salt solution.)

TABLE I.

Source of blood	Initial pressure of O_2 in gas bag	Partial pressure of O_2 in blood by micro method
Dog	116	117
,,	124	123
,,	141	142
,,	127	127
,,	131	130
,,	142	138
Human	127	122
,,	118	113

The accuracy of the method was checked by experiment on the blood of dogs and men. Samples were equilibrated with gas mixtures whose oxygen content was known. Then the oxygen tension in the liquid was determined by this method. The results are shown in Table I.

The determinations on normal people also constitute a check on the accuracy of the method. The results on this group are shown in

TABLE II.

Patient	Oxygen saturation in %	Oxygen partial pressure in mm.
N	97.2	76
,,	97.4	81.0
M.C.	95.0	83.5
P.	96.4	80
P.A.	95.6	82
W.	96.2	74
R.	96.8	88
S.	95.4	76
,,	95.4	75
Mean	96.1	79.5

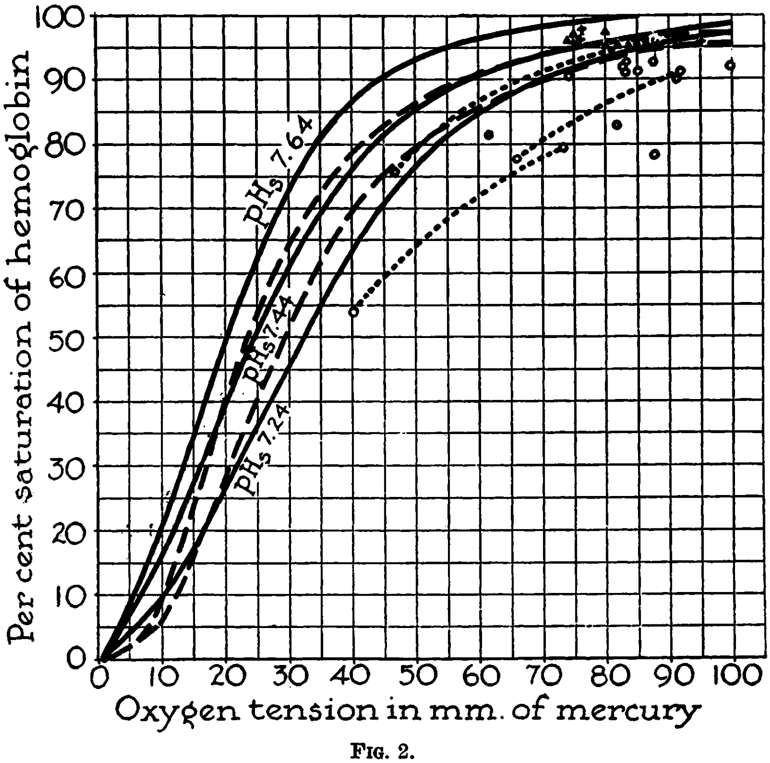

FIG. 2.

The solid line curves are the oxyhemoglobin dissociation curves for the stated pH figures (Henderson). The broken lines are the normal limits of the curves after Barcroft. Normal results from Table II are shown by the triangles and crosses. The circles show an anoxemic situation (Table III). The dotted lines connect successive determinations on the same patient.

Table II. The data from the table is shown on the graph in Fig. 2 in comparison with the normal limits of oxyhemoglobin dissociation curve[3] and the curves for various pH figures.[4, 6] Nine complete studies were carried out on subjects who were hospitalized for non-respiratory conditions and who had no circulatory abnormalities. The O_2 saturation was determined while measurement of the tension of the same sample was in progress. The average O_2 saturation was 96.1%. The average O_2 tension was 79.5 mm.

TABLE III.
Patients with Oxygen Want.

Patient	Arterial oxygen saturation in %	Partial pressure of oxygen
R.	76.2	47
G.	79.4	73
	54.6	40
Gil.	92.2	85
K.	82.2	62
W.E.	91.1	83
C.	93.0	87
	78.0	87
H.	93.0	83.6
S.	92.0	92.6
V.N.	91.0	74
	83.0	82
	92.4	100
Wal.	77.5	66
	90.5	91.5
Sm.	91.9	83

In Table III the presence of an anoxemia in 11 patients with various diseases is shown by an arterial oxygen saturation below 93%. It is apparent from a glance at Fig. 2 that the oxygen tension figures are higher than correspond to the normal limits of the oxyhemoglobin dissociation curve. In patients G. and W. oxygen by nasal catheter was stopped for a time to produce the extreme anoxemia indicated in Table IV. T. W. had an acidosis from a uremia which may have accounted for part of the shift from the expected position of the curve. Patient C., with no anoxemia, shows a normal O_2 tension for the O_2 concentration determined while breathing a low oxygen atmosphere. Observations of such abnormally elevated partial pressures of oxygen are not unique. Henderson[4] observed it in such unrelated diseases as pernicious anemia, nephritis and myxedema. Litarczek[5] records it in experimental anemia of rabbits and in anemic patients. Various physico-chemi-

[4] Henderson, J. J., *Blood*, New Haven, 1928, p. 285.
[5] Litarczek, G., Aubert, H., and Cosmulesco, I., *C. R. Soc. Biol.*, 1929, **101**, 220.
[6] Richards, D. W., Jr., and Strauss, M. L., *J. Clin. Invest.*, 1926, **4**, 105.

cal factors control the oxygen combining power of hemoglobin. The K of the Hill-Barcroft equation is known to vary, however, with different bloods at identical temperatures and hydrogen ion concentrations.[7] These fluctuations may be wide and of importance in pathological states.

Conclusions. 1. A modified aerotonometer method for determining the partial pressure of oxygen can be applied to blood drawn from a human artery and is reasonably accurate. 2. In patients thought to be normal a certain variation obtains. 3. Partial pressure results which are high in relation to the oxygen saturation are commonly seen in the presence of anoxemia.

8461 C

Intravaginal Assay of Urinary Estrin.

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Since estrin is not commonly standardized on the basis of its ability to produce behavioristic estrus, but rather by virtue of its growth-promoting influence on the vaginal epithelium, there seems but little need to saturate the entire animal to gain this end. The vaginal epithelium reacts to extremely minute quantities of estrin applied locally,* although Pratt and Smeltzer[1] and Powers, *et al.*,[2] found their methods of vaginal administration only one-third to one-half as efficacious as the subcutaneous.

We have used the intravaginal method of assaying urinary estrin not only because minute amounts may be detected (even in male urine), but also to avoid the toxic effects produced by parenteral injection of crude extracts. Twenty-four-hour urines were obtained from 4 women† on days 7, 14, 21, and 28 of the menstrual

[7] Judd, E. S., Snell, A. M., and Hoerner, M. T., *J. A. M. A.*, 1935, **105**, 1653.

*Cornification of the vaginal epithelium (without uterine growth) may be produced by vaginal administration of 1/200th of a rat unit of "Progynon" (kindly supplied by the Schering Corporation, New York).

[1] Pratt, J. P., and Smeltzer, M., *Endocrinol.*, 1929, **13**, 320.

[2] Powers, H. H., Varley, J. R., and Morrell, J. A., *Endocrinol.*, 1929, **13**, 395.

† We are indebted to the Nursing Department of the Providence Hospital, Oakland, California, for obtaining urine samples from 4 nulliparous nurses from 19 to 21 years of age. Their physical and dietary habits were as equal as hospital routine would allow. They had normal menstrual cycles varying from 25 to 29 days with the period of flow varying from 4-6 days. Cases 3 and 4 had acne vulgaris, otherwise no gross deviations from the normal were observed.