dominated in the bone marrow.

Urethane has been observed to inhibit mitotic activity in the corneal epithelium of the rat,[4] and similar effects have been noted for other cells in tissue culture.[5] Consequently counts of mitotic figures were made on the bone marrow of normal and leukemic mice before and after administration of urethane. No inhibition of mitosis in myeloid cells could be detected 11 hours after a single injection of urethane into normal mice (6 animals). Fewer mitotic figures were present, however, in the marrows of urethane-treated leukemic mice (11-24 hours after last injection) than in controls (29 mitotic figures for 40 oil immersion fields of untreated leukemic marrows—range of 12 to 42, 14 mitoses in treated marrows—range of 7 to 30). This is not interpreted necessarily as meaning that mitosis had been inhibited by the drug, since there were fewer cells in the urethane-treated marrows capable of undergoing mitotic division.

As a result of the action of urethane many mature cells appeared in the bone marrow. With the release of these cells instead of immature leukemic cells into the blood, the circulating population of white blood cells had a shorter life expectancy. Thus, a great per cent of the circulating cells were probably dying within a relatively short time after release from the marrow. This is not offered as the probable sole explanation for the depression in the white blood cell count of myeloid leukemia following urethane therapy, since other factors such as rate of release of cells from the marrow and peripheral destruction may be involved.

These animals with myeloid leukemia represent an excellent test object for determining the ability of drugs chemically related to urethane to produce similar effects on myeloid leukemia.

Summary. The administration of a single anesthetic dose of urethane resulted within 24 hours in a drop in the white blood cell count and the appearance of many mature cells in the bone marrow of leukemic mice. Since the number of mitotic figures in marrow myeloid cells was decreased, maturation may have been secondary to inhibition of mitosis in blast cells. However, in the treated mice there were fewer marrow cells capable of undergoing division, which may account for the reduced number of mitoses. The release of an increased per cent of mature cells into the circulating blood may be a factor in depression of the white blood cell counts following the injection of urethane into mice with myeloid leukemia.

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The Oxigram as a Measure of Cardiorespiratory Reserve.*

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Most of the available methods for determining the functional reserve of the cardiorespiratory system have objectionable features.[1-6] A new test was suggested by the consideration that in disease of the heart or

* Aided by a grant from the Dazian Foundation for Medical Research.

1 Nylin, G., *J. A. M. A.*, 1937, **109**, 1333.

2 Schneider, E. C., *J. A. M. A.*, 1920, **74**, 1507.

3 Master, A. M., *Am. Heart J.*, 1935, **10**, 495.

4 Master, A. M., Friedman, R., and Dack, S., *Am. Heart J.*, 1942, **24**, 777.

5 Levy, R. L., Bruenn, H. G., and Russell, N. G., Jr., *Am. J. Med. Sc.*, 1939, **197**, 241.

TABLE I.
Analysis of Oxigrams of 6 Normal Subjects and of 3 Patients. The normal values in the cardiac patient (V.P.) with good estimated reserve (class IB) are to be noted.

Subject	Diagnosis*	Lowest O_2 saturation during 5 min. hypoxia	"O_2 Unsaturation Min." during 5 min. hypoxia
S.B., ♂, 23 yrs	Normal	82.5	62.6
C.E.K., ♂, 37 "	"	87.0	34.0
J.B., ♀, 38 "	"	89.5	38.5
B.G. ♂, 21 "	"	81.0	70.0
H.N., ♀, 22 "	"	91.5	29.0
A.H., ♂, 25 "	"	84.0	56.0
		Mean 85.9	Mean 48.4
V.P., ♂, 23 "	Inactive rheumatic heart disease, class IB	88.0	39.4
W.O'B., ♂, 65 "	1. Hypertensive and arteriosclerotic heart disease, class IVD 2. Pulmonary emphysema	65.0	142.8
L.B., ♂, 81 "	1. Arteriosclerotic and hypertensive heart disease, class IVE 2. RLL pneumonia	75.0	91.0

* Functional and therapeutic diagnoses in accordance with "Nomenclature and Criteria for Diagnosis of Diseases of the Heart."

of the lungs the form of hypoxia encountered is of the hypoxic or stagnant type, or a combination. In either, the extent of the abnormality is reflected in the degree of hypoxemia. A continuous record of the oxygen saturation of the arterial blood in response to the inhalation of gaseous mixtures with different tensions of oxygen might give a quantitative measure of the efficiency of oxygen transport, and in turn of cardiac and of respiratory function and functional reserve. A record of the kind in question we have termed the "oxigram."

An oxigram is easily made with the aid of Millikan's oximeter.[7] The method is quite accurate, for simultaneous determinations on normal subjects[8] at various levels of oxygen saturation down to 60% by means of the oximeter and of the gasometric method[9] have revealed differences usually within $\pm 5\%$.

Adaptation to a Clinical Test. Low oxygen tension mixtures as a means of testing the efficiency of the hemal oxygenating mechanisms were administered. The procedure was as follows: The galvanometer having been adjusted, the photometer was placed on the ear of the sitting subject or patient. For 15 or 20 minutes, 100% oxygen was breathed through a BLB mask (Army Air Forces type A-8B)† and when no further rise of the galvanometric deflection occurred the subject's arterial blood was assumed to be saturated 100% of capacity. The mask was removed and room air breathed until the galvanometer levelled off. The mask was then replaced and connected to a source of gas containing 10% oxygen (pO_2 approximately 76 mm Hg) and 90% nitrogen (pN_2 approximately 684 mm Hg). In normal subjects this mixture was breathed as long as possible, but in patients the degree of hypoxemia induced could not be tolerated for more than 5 minutes. It is probable, therefore, that as finally evolved the test period

6 Caughey, J. L., PROC. SOC. EXP. BIOL. AND MED., 1935, **32**, 973.

7 Millikan, G. A., *Rev. Sc. Instruments*, 1942, **13**, 434.

8 Hemingway, A., and Taylor, C. B., *J. Lab. and Clin. Med.*, 1944, **29**, 987.

9 Van Slyke, D. D., and Neill, J. M., *J. Biol. Chem.*, 1924, **64**, 543.

† This mask probably does not deliver the exact percentage of gas found in the oxygen bottle attached to it. See reference.[10]

10 Army Air Forces Manual No. 25-0-1, Nov., 1945, and Manual No. 25-2, 15 March, 1945, Headquarters, Army Air Forces, Washington, D.C.

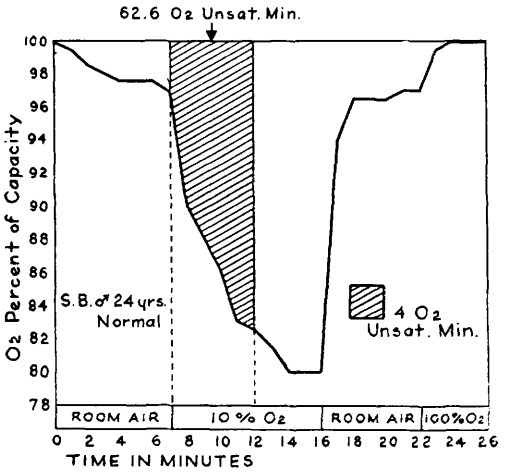

FIG. 1.
Oxigram of a young normal subject.

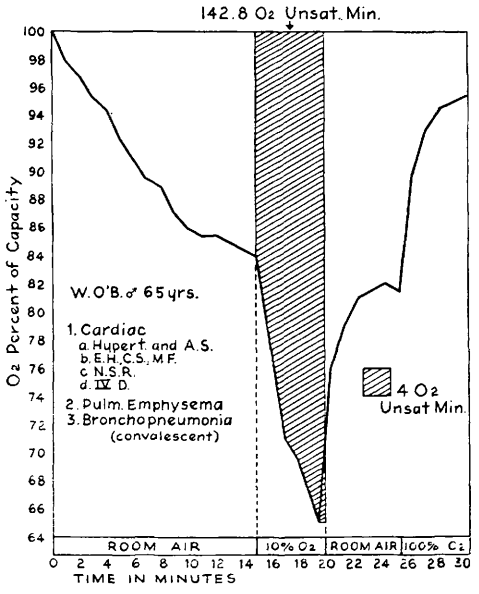

FIG. 2.
Oxigram of a cardiac patient convalescing from bronchopneumonia. The oxygen-deficient mixture could not be breathed for more than 4.5 minutes. The 5-minute area was completed by merely extending the lowest oxygen saturation reached to the end of the fifth minute.

will be limited to 5 minutes in duration since even in normal subjects, the steepest part of the unsaturation curve is encountered in this time. Following the test period, room air was breathed again until pretest levels were reached. Finally 100% oxygen was given by mask for several minutes, largely as a check on the accuracy of the apparatus.

Results. Representative oxigrams are shown in Fig. 1 and 2 and the results obtained in 6 normal subjects and in 3 patients are shown in Table I. The differences between the normal (Fig. 1) and the cardiac with good reserve (Table I) on the one hand, and the patient with poor cardiac reserve on the other (Fig. 2) are immediately apparent. Particularly notable in the latter are the considerable fall of the curve while the patient was breathing room air; the depth to which the curve descended during the actual test period; and the sluggish return to pretest levels when the patient was permitted to breathe room air again.

In order to get a measure of the rate as well as depth of fall of the oxigram in response to induced hypoxemia various areas of the curve in units of "oxygen unsaturation minutes" were measured with a planimeter. Taking the immediate prehypoxic level of oxygen saturation as a base it was found that the area of the curve during 5 minutes of hypoxia did not differ greatly in normal subjects and in patients with cardiopulmonary disease. Clearly, however, a sufficient number of cases have not been tested. In order to include into a single measurement the oxygen unsaturation that occurred when the subjects were breathing room air and when they were breathing low oxygen mixtures, the area of the test curve was extended to the baseline of 100% saturation (see shaded areas in figures). There was then, of course, considerable difference between patients with poor reserve and normal subjects.

Establishment of the reliability of the procedure, and correlation with other measures of cardiac and respiratory function remain to be done.

Summary. A graph in which oxygen saturation of the arterial blood is plotted against time while the subject is breathing different concentrations of oxygen in a standard sequence is termed an "oxigram." Preliminary observations indicate that the oxigram may be useful for measuring cardiorespiratory reserve.

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