covered in the urine 24 hours after giving 100 mg/kg, intragastrically. Since less than 10% of the dose was recovered concomitantly from the gastrointestinal tract and its contents, it is concluded that for the most part phenindamine is completely metabolized in the body.

Summary. Phenindamine (Thephorin) was determined in biologic material with a high degree of specificity by a modification of the Brodie methyl orange technic. Negligible amounts of phenindamine can be recovered in the urine of humans following oral administration. In studies on rats the compound appears to be rapidly absorbed from the gastrointestinal tract. The compound rapidly leaves the blood and concentrates in tissues. High concentrations of the drug were found in the lungs, liver, kidneys and brain. Extensive accumulation of phenindamine did not occur after repeated administration of the compound twice daily for 4 consecutive days. It is concluded that the compound is metabolized to a considerable extent in the body since less than 12 per cent of the total dose of phenindamine could be recovered unchanged in the urine and feces 24 hours following oral administration.

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Relationships of Vital Capacity and Ventilatory Measurements to Physical Fitness in Patients with Cardio-Respiratory Diseases.* (17920)

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Previous studies have shown a direct relationship between physical fitness scores of working capacity and the availability of oxygen to the tissues in an heterogeneous group of ambulatory patients with cardio-respiratory diseases(1). The clinical evaluation of disability in these patients varied from virtually none to complete and total disability, with the majority comprising the intermediate ranges. Physical fitness was scored from an integration of the most reproducible characteristics of circulatory and pulmonary performance during standardized exercise. The first of these was the duration of time that moderate exercise on a treadmill ergometer could be tolerated (up to an arbitrary maximum of 10 min.). The other criteria were the mean respiratory efficiency (volumes % of oxygen absorbed per unit volume of air ventilated) during exercise, and the total number of heart beats for the first 3 minutes of recovery(2). Others have found significant relationships of the vital capacity, the maximum breathing capacity and the breathing reserve to the awareness of dyspnea in patients with pulmonary diseases(3, I-III). In view of these considerations, it becomes important to ascertain how well vital capacity, and various measures of ventilatory performance commonly used in evaluating

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1. Bruce, R. A., Lovejoy, F. W., Jr., Yu, P. N. G., and McDowell, M., PROC. SOC. EXP. BIOL. AND MED., 1950, v73, 212.

2. Bruce, R. A., Lovejoy, F. W., Jr., Yu, P. N. G., and McDowell, M., Pearson, R., *Science*, 1949, v110, 442.

TABLE I.
Relations of Ventilatory Measurements to Physical Fitness.
(Simultaneous values in 44 patients).

Factors	Mean ± St. dev.	Range, min.–max.	Coef. of variation, %	Coef. correlation with physical fitness index, r ± st. error*	p, %
Physical fitness index†	11.6 ± 5.4	1.3– 21.5	46.6		
Vital capacity, Obs. × 100 / Pred.	73.3 ± 19.3	21 –105	26.3	+.587 ± .099	<.0001
Max. mask breathing capacity, L/m²/m	24.7 ± 7.4	8.3– 39.2	30.0	+.395 ± .128	<.27
Mean exercise ventilation, L/m²/m	9.46 ± 2.08	4.2– 13.4	21.9	—.021 ± .145	
Breathing requirement, %	41.4 ± 14.8	19 – 79	35.7	—.477 ± .117	<.006
" reserve, %†	58.8 ± 14.6	21 – 81	24.8	+.458 ± .120	<.014
Mean exercise mid-capacity, pCO_2, mm Hg	33.7 ± 7.5	20 – 52	22.2	+.410 ± .126	<.13
Ventilation, % of total	73.2 ± 9.5	54 – 88	12.9	+.181 ± .147	<23

* Standard error of coefficient of correlation equals $\frac{1-r^2}{\sqrt{N-1}}$

† The mean normal values of the physical fitness index and breathing reserve at 1.73 mph. level walking are 18.9 ± 2.8 and 71.6 ± 6.4, and at 2.6 mph. level walking, 19.4 ± 3.8 and 74.8 ± 4.6, respectively.

pulmonary function, correlate with the physical fitness index in patients selected at random.

Methods. For this purpose the exercise data on 44 patients with a variety of cardiorespiratory diseases have been analyzed. They ranged in age from 15 to 61 years. The chief clinical categories of disease represented were: congenital cardiovascular disease, 8; acquired heart diseases, 12; pulmonary diseases, 16; and miscellaneous diseases affecting cardiorespiratory functions, 8. Vital capacity was measured in the usual manner, and expressed as per cent of the predicted values for age, sex, and height(3, I). The maximum mask breathing capacity was obtained at the end of the treadmill test in order that the breathing requirement‡ and reserve values would be based upon the same equipment of face mask and valves as were used for the ventilation measurements during exercise. (Since high velocity valves were not employed, the values were lower than those generally reported in the literature, and the mean normal value for adults was 29.8 ± 5.6 liters per square meter of body surface area per minute, STPD). The exercise tests (*level* walking) were the same as described previously(4). Since the degree of disability varied from almost none to complete, 24 patients were able to walk for 10 minutes at 2.6 m.p.h., 9 were able to walk for 10 minutes at 1.73 m.p.h., and the remainder were unable to complete the prescribed period of 10 minutes at either speed tested. The mid-capacity (intra-pulmonary) ventilation percentage was derived from:

$$\frac{\text{Insp. } O_2\% - \text{Exp. } O_2\% \times 100}{\text{Insp. } O_2\% - \text{Mid-capacity } O_2\%}$$

3. (I) Baldwin, Cournand, Richards, D. W., Jr., *Medicine,* 1948, v27, 243; (II) Baldwin, Cournand, Richards, D. W., Jr., *Medicine,* 1949, v28, 1; (III) Baldwin, Cournand, Richards, D. W., Jr., *Medicine,* 1949, v28, 201.

‡ The breathing requirement equals:

$$\frac{\text{average exercise minute ventilation volume}}{\text{maximum mask breathing capacity}} \times 100$$

whereas the breathing reserve equals 100 minus the breathing requirement. Gas volumes are corrected to square meters of body surface area, STPD, to aid estimation of oxygen consumption(4).

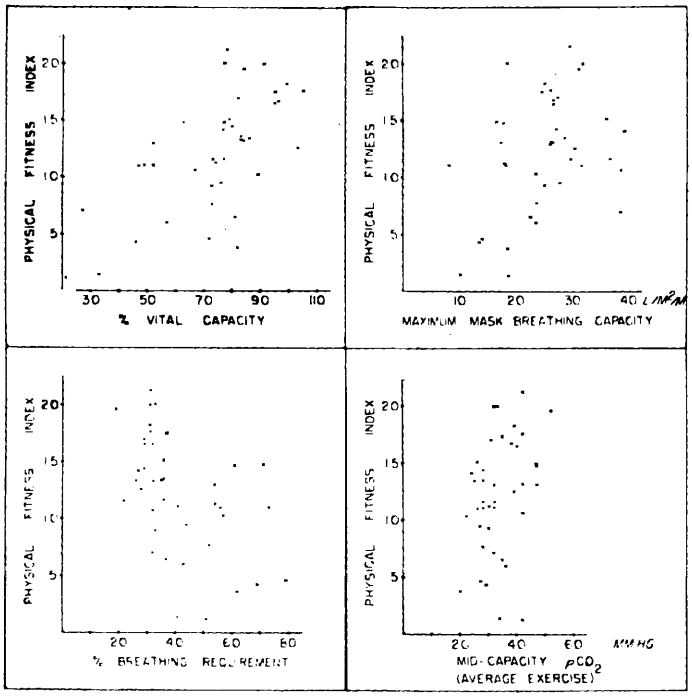

FIG. 1.

Relationships of the physical fitness index to the percentage vital capacity, maximum mask breathing capacity, percentage breathing requirement and mid-capacity (mixed alveolar) pCO_2 during exercise.

Hence, the percentage dead space ventilation equalled 100 minus the percentage mid-capacity ventilation. Statistical correlations were made by the product-moment method, and scatter graphs of significant relationships are included. The awareness of dyspnea, and the relative intensity of distress were evaluated in each patient.

Results. The statistical analyses of the results obtained are presented in Table I. The least variable factor was the percentage mid-capacity ventilation during exercise. This represented the intra-pulmonary portion of the total ventilation, whereas the remainder represented the ventilation of the physiological dead space. The most variable factor was the physical fitness index. A significant relationship was found between the physical fitness index and the vital capacity expressed as the percentage ratio of the observed to predicted volumes (Fig. 1). Relationships of lesser significance were also demonstrated between the physical fitness index and the maximum mask breathing capacity, breathing requirement and breathing reserve, as well as the mean exercise mid-capacity (mixed alveolar) pCO_2. Neither the average minute ventilation, nor the mid-capacity portion of the total ventilation, showed any relationship to the fitness index.

Whereas only 30% of the patients who were able to walk for 10 minutes experienced dyspnea, all patients who were unable to walk for 10 minutes complained of dyspnea. In general, the more intense the dyspnea, the more marked was the observed reduction in exercise tolerance.

Comments. Of the several ventilatory measurements appraised in this heterogeneous group of patients, more or less disabled by cardio-respiratory diseases, the percentage vital capacity showed the best correlation

4. Bruce, R. A., Lovejoy, F. W., Jr., Pearson, R., Yu, P. N. G., Brothers, G. B., and Velasquez, T., *Clin. Invest.*, 1949, v28, 1423.

with the physical fitness index of exercise performance. The vital capacity has been expressed in these terms in order to correct for variations in individuals due to age, sex, and height. This relationship to the ability to perform moderate exercise of level walking is not a perfect one, however. Some patients with either acquired or congenital heart disease may have appreciable venous admixture via abnormal channels, or perfusion of inadequately ventilated alveoli, which permits incomplete saturation of the arterial blood with oxygen. Thus these individuals may have diminished exercise tolerance from hypoxemia independent of significant changes in vital capacity. Furthermore, the vital capacity volume may be a poor index of exercise performance in some emphysematous patients who exhibit a nearly normal vital capacity volume, but are unable to expel the air at a normal velocity because of diminished pulmonary elasticity. In such individuals the maximum breathing capacity is reduced and affords a more reliable appraisal of ventilatory performance. In this heterogeneous group of randomly selected patients, it should be noted that the breathing requirement showed a correlation with the fitness index which the mean exercise ventilation volume failed to exhibit.

Although in a previous study the physical fitness index was found to be proportional to the physically dissolved oxygen in the blood(1), we have not been able to demonstrate a direct relationship between the vital capacity and the arterial pO_2. Nevertheless, the simplified measure of working capacity used herein may reveal relationships to some of the physiological factors, which in an integrated fashion, determine the overall capacity for exertion. The interrelations of such factors, however, do not always follow because of the multiplicity of pathological processes which are responsible for functional impairment.

Summary. Simultaneous analyses of various ventilatory measurements in 44 randomly selected patients with cardio-respiratory diseases have been assembled. A significant relationship was found between the physical fitness index and the percentage ratio of the observed to predicted vital capacity. The limitations of this relationship, as well as other relationships of physical fitness score to various ventilatory measurements, are discussed.

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Cardiovascular Changes Induced by Rapid Expansion of the Extracellular Fluid. (17921)

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It has been shown(1) that marked alterations in glomerular filtration rate and renal blood flow follow the expansion of extracellular fluid which occurs when large volumes of a modified Locke's solution are infused intravenously in dogs. In order to assess the role of general cardiovascular changes in this response we have examined vascular pressures and volume during and after such infusions.

Methods. Two series of observations were made on each of 4 trained, unanesthetized female dogs weighing 12 to 15 kg. In 5 experiments 1100 cc, and in 3 experiments 1600 cc, of a modified Locke's solution* were

1. Wesson, L. G., Anslow, W. P., Jr., Raisz, L. G., Bolomey, A. A., and Ladd, M., *Am. J. Physiol.*, in press.

* The solution contains 153 mEq/l of sodium, 134 mEq/l of chloride, 27 mEq/l of bicarbonate, 4 mEq/l of potassium, 4 mEq/l of calcium, and 100 mg/100 cc of glucose.