Physiological Measurements of Metabolic Functions in Man

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PREFACE

The number of methods of measurement that can be used in the study of the phenomena of metabolism is very large. Although almost all of the chemical methods of analysis will eventually be replaced by physical methods, and automation will make possible a large increase in the amount of data secured, most of the actual physiological procedures and calculations cannot be changed. In this sense, analytical procedures are secondary, the physiological procedures primary.

The authors of this book have been particularly interested in human bioenergetics, respiratory metabolism, cardiopulmonary function, environmental physiology, and work physiology. The methods described in this compilation of procedures for studying respiratory metabolism and procedures that are applicable in detecting changes in body composition have worked satisfactorily in the authors' laboratories and have been chosen primarily because of their reliability, simplicity, and reproducibility. In general, a brief discussion of the principles and background of each method precedes the details of the methods.

The first portion of the book, Sections 1 through 5, deals with respiratory metabolism and some aspects of the physiology of blood and of pulmonary function. From such data oxygen consumption and carbon dioxide production may be computed, respiratory function may be followed, and acid-base balance may be quantified.

The middle portion, Sections 6 through 8, deals with body composition and metabolic balances. The emphasis here is on the total weight of the body, the water content of the body, and the various gross fractions: protein, fat, carbohydrate, and other solids.

Sections 9 through 13 deal with what is sometimes called "applied physiology," although the authors are not certain that there are logical distinctions between "basic," "pure," and "applied" physiology. In any case the important areas of physical fitness and environmental physiology, with some comments on meteorological measurements and metabolic statistics, comprise this portion of the book.

The final discussion, Section 14, prepared by Dr. Frederick Sargent, II, and Mrs. Karla P. Weinman, considers the limits of variability of some functions in man and the fundamental concept of homeostasis.

Although clinical applications are not dealt with specifically, it is clear that virtually all the methods described either have had or can have clinical application. Indeed, some of them have come straight from the clinic into the physiology laboratory.

The reader should have no difficulty in locating the standard books, monographs, and journal articles listed in the references, but he undoubtedly will have difficulty in locating the research reports of military laboratories. The authors can only suggest that the reader may be able to secure microfilms of such reports from the National Medical Library, Bethesda, Maryland, or from the Office of Technical Services, Department of Commerce, Washington, D.C.

Some of the material in this book was taken from our previous books, which include *Laboratory Manual of Field Methods for the Biochemical Assessment of Metabolic and Nutritional Conditions* (Johnson, Sargent, Consolazio, and Robinson; Harvard Fatigue Laboratory, Boston, 1946); and *Metabolic Methods* (Consolazio, Johnson, and Marek; the C. V. Mosby Company, St. Louis, 1951).

In acknowledging debts of gratitude, the authors wish to thank first all colleagues, past and present; particularly, Lawrence J. Henderson, David Bruce Dill, Arlie V. Bock, John H. Talbott, William V. Consolazio, William H. Forbes, Sid Robinson, Robert C. Darling, H. S. Belding, and Frederick Sargent, II. We are grateful as well for the help and advice of Drs. Morton I. Grossman, William Insull, Luke Pascale, William R. Best, and members of the Bioenergetics Division of the United States Army Medical Research and Nutrition Laboratory. Colonel Laurence M. Hursh, MC, former commanding officer of USAMRNL, gave us continuous encouragement and understanding during the preparation of this book.

Mr. Carl E. Gordon efficiently redrew the line charts; Mrs. Frances Robbins gave invaluable assistance in the final assembly of the bibliography and in checking the proofs, and Mrs. A. Marie Robinson rendered a great service as grammarian, proofreader, and typist in the preparation of the manuscript.

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Section 1

RESPIRATORY METABOLISM

CALORIMETRY

The production of heat or energy by the human body is measured by the use of both direct and indirect calorimetry. Each of these techniques has its particular advantages and disadvantages. It has been shown that calorimetry is of value in the diagnosis and treatment of disease, in the evaluation of nutritional requirements for various occupations, and in the design of efficient tools, equipment, and work methods.

Man is dependent exclusively upon food for his source of energy. The quantity of energy used normally is reflected either by a gain in body weight as energy is stored or by a loss in body weight as the body consumes itself for fuel.

The units for energy are the same units used to express work. Energy is defined as the capacity for performing work, and work is the transference of energy by a process involving the movement of a solid body through space. Therefore, work is expressed as the force times the distance, or simply as the force acting upon a body to produce motion, times the distance through which it acts.

Among the many units used for expressing work are calories, both small and large. Whenever Calories are discussed without qualification, reference is made to the large Calorie or the kilocalorie, which is defined as the amount of heat required to raise the temperature of 1 kg of water, 1°C. Another term used for expressing the energy equivalent is the kilogram-meter, which is, simply, the amount of work performed when a body of given weight is moved against gravity through a known distance. As an example, if an individual raises a 3-kg weight through 3 meters, then he has performed 9 kg-meters of work.

The measurement of energy expenditure is referred to as calorimetry, in which energy is measured as heat, heat being one of the most conveniently handled forms of energy. Calorimetry is based on the law of the conservation of energy This law states that energy can neither be created nor destroyed, and therefore the energy content of any system can be increased or decreased only by the amount of energy that is added or subtracted from the system. Whenever work can conceivably be derived from a system, then, by definition, potential or kinetic energy is present in that system.

Potential energy is defined as either the energy of position of a body (a book on a table possesses energy by reason of its position and it can perform work if it falls off the table) or the potential chemical energy of certain substances.

Kinetic energy, the other general type of energy, has various forms, such as heat, light, and motion. It is the energy of movement, and it is the work that can be performed by moving bodies.

Calorimetry, as applied to studies in man, is divided into two types. Direct calorimetry is the measurement of energy expenditure in the form of heat; all types of energy are converted to heat and then measured. Since energy is utilized in the human body by means of chemical reactions, it is possible to evaluate energy utilization from the measurements of the substances consumed and the products formed. In indirect calorimetry, the second type of calorimetry, energy expenditure is determined from the amounts of oxygen consumed and carbon dioxide produced.

Direct Calorimetry

Direct calorimetry depends on the measurement of energy as heat. The calorimeter required for this measurement consists principally of a box-like chamber containing multiple-layer walls, including a series of cold water pipes for cooling, electrical elements for heating, and thermocouples for measuring the temperature. By proper manipulation of the calorimeter, the temperature across the walls can be maintained constant and any heat loss can be prevented. The heat produced by the subject in the chamber is absorbed by the series of circulating water pipes inside the chamber and is then measured by recording the increase in the water's temperature. The interior of the chamber is ventilated by its own closed system of air ducts with a fan. The heat expended by the subject in vaporizing water from the lungs and skin surfaces is determined by trapping the vapor in a condenser and weighing the water. Any changes in the heat content of the body of the test subject are estimated from the changes in the body temperature. In the chamber the energy expenditure of a man can be measured in the form of radiant heat, heat of vaporization, work on a bicycle ergometer, febrile increase of the body temperature, or heat produced by walking about in the chamber. Small models of the constant-temperature calorimeter have been used to measure resting metabolism, while the larger models have been used to measure the energy expenditure of work. However, this apparatus is expensive to construct and difficult to operate, and its size usually restricts the various metabolic activities. The apparatus can be converted into a constant-temperature respiratory calorimeter by the addition of a closed circuit for air ventilation, and as a result all the carbon dioxide produced and all the oxygen consumed by the subject can be measured. The outstanding advantage of this apparatus is that the total metabolism of a man can be measured by evaluating the balance of all forms of matter and energy that enter and leave the subject. Food can be passed in and urine and feces passed out without disturbing the conditions of the chamber by using special doors in the chamber walls.

Indirect Calorimetry

In measuring energy expenditure indirectly, the known proportionality between the oxygen consumption or the carbon dioxide production and the total energy production is used. This method for measuring energy expenditure is also referred to as respiratory calorimetry. It is performed in two ways. In the open-circuit method, the subject is permitted to breathe air from the outside, while his expired air is collected in either a gasometer or metabolimeter for volumetric measurement. This gas volume is corrected for standard conditions and is analyzed for its oxygen and carbon dioxide content, with the subsequent calculations of oxygen consumption and carbon dioxide production. In the use of the closed-circuit method, the subject is completely cut off from the outside air and breathes through a closed system. The respirometer originally contains pure oxygen. As the gas is expired by the subject, the carbon dioxide is constantly removed as it passes through soda lime. The decrease in the gas volume, in this closed system, is related to the rate of the oxygen consumption, from which the metabolic rate is then calculated

Human Calorimetry by the Gradient Principle

A third type of human calorimetry, using the gradient principle, has been employed. The principle described by Benzinger et al. (1958) can be paraphrased as follows:

> Let us assume that the surface of a cavity is thoroughly lined with a layer of material that is of uniform thickness and thermal conductivity. Once a steady state of heat flow is reached, the integrated difference or gradient of temperatures between the inner and outer surfaces of this layer is proportional to the rate of total heat loss or heat gain from any source within the cavity. During a change from one constant heat flow rate to another, the temperature gradient shows a rapid exponential rise or fall to a new level, which then represents the new steady heat flow rate. Since thick layers of material produce a high gradient, they will reach a steady state much more slowly. The thin layers have a faster but a much less sensitive response.
>
> The integrated response, in terms of the temperature gradient, has been shown to be independent of the size, shape, location, emissivity, and distribution of temperature over the surface of the heat source. This is due to the fact that the

geometry delineated by the gradient layers has the essential properties of a black body for any incident thermal energy. Any closed surface, irregular or regular, large or small, surrounding the source of heat and intersecting its total thermal gradient field, will intercept on its passage, the total energetic output from the source. This is providing that there is no change of total enthalpy within the closed space. The integrated response is also independent of the manner in which heat is transferred to the layer, whether by conduction-convection, radiation, or condensation of the water vapor that has previously been generated at the surface of the heat source.

Discussion of the Methods for Calorimetry

Atwater and Benedict (1903), Benedict and Milner (1907), and Gephart and Du Bois (1915) have shown that when the constant temperature respiration calorimeter is used, the methods for direct and indirect calorimetry are in agreement and can therefore be used in determining the rate of energy expenditure.

Since the indirect calorimetry methods do not measure heat production directly, the heat equivalents of the oxygen consumed and carbon dioxide produced must be determined. The heat produced when one consumes 1 liter of oxygen varies with the foodstuff burned as fuel. For example, the combustion of 1 liter of oxygen produces 4.68 kcal of heat with fat alone, 5.05 kcal with the carbohydrate starch alone, and 4.48 kcal with protein alone. Correspondingly, the heat evolved in the production of 1 liter of carbon dioxide varies with the foodstuff consumed; and, as one expects, varying proportions of different foodstuffs in the fuel will result in a varying heat production per liter of oxygen. In addition, the proportion of the oxygen consumed to the carbon dioxide produced per unit of weight will vary with the types of food consumed. This is expressed as the ratio of the volume of carbon dioxide produced to the volume of oxygen consumed, and it is called the respiratory quotient or RQ.

Errors in the use of indirect calorimetry may arise by divergence from the assumed conditions. The Zuntz-Schumburg tables of caloric equivalents for fat-carbohydrate combustion mixtures are based upon combustion characteristics of a specific fat or carbohydrate. If a different fat or carbohydrate dominates the combustion mixture, the caloric values may not apply, and the calculations will be in error. The tables were derived for use in respiration calorimetry, in which gaseous exchange across the skin is measured. When a mask or mouthpiece is used, skin respiration is missed, and a falsely low energy expenditure results. Generally, these errors are not significant and may be disregarded. However, the use of the nonprotein RQ in determining the kilocalorie equivalent of the oxygen may lead to error if the RQ itself is not representative of the combustion mixture. This occurs during the onset of acidosis or alkalosis when carbon dioxide transport is disrupted and carbon dioxide excretion is increased or decreased, respectively. This error rarely arises in the normal resting state, but it is encountered in disease and during exercise, at the beginning and during recovery.

The methods of measuring energy expenditure have numerous practical and theoretical applications. Each method has advantages and disadvantages which govern its use in specific applications. The technique of direct calorimetry with the chamber and ancillary equipment of the constant temperature respiration calorimeter is cumbersome, time-consuming, and expensive. Yet it is accurate and permits extended observations though of a rather limited range of activities. Indirect calorimetry is much more convenient since the equipment can be portable, relatively inexpensive, almost self-analyzing, and under defined conditions as accurate as direct calorimetry.

Atwater and Benedict (1903) and their group applied the modern-day techniques of direct and indirect calorimetry to the demonstration of the validity of the law of conservation of energy for the human organism by first using carbon dioxide production as a measure of gaseous exchange and later using oxygen consumption [Benedict and Milner (1907)]. In their experiments they showed that the energy intake balanced the energy expenditure within 0.1 per cent. The confirmation of the law of conservation of energy placed calorimetry upon a secure basis.

Because of the difficulty of performing direct calorimetry, it was important to show that indirect calorimetry was as accurate as the direct method. Comparative studies were performed on both animals and man. For example, in one series of experiments comparing both methods, there was agreement within 0.17 per cent of each method over a range of RQ between 0.77 and 0.97 [Gephart and Du Bois (1915)].

Following the confirmation of results showing the validity and accuracy of calorimetry, studies were performed in two areas, the measurement of metabolic rate in health and disease and the measurement of energy expenditure.

RESPIRATORY METABOLISM: CALCULATIONS

Reference

Haldane, J. S., and Priestley, J. G.: Respiration. New York, Oxford University Press, 1935.

Principle

From the pulmonary ventilation and the carbon dioxide, oxygen, and nitrogen content of the expired air that is compared with the inspired air, the oxygen consumption and carbon dioxide production are calculated. From these data energy expenditure is subsequently computed.

Pulmonary Ventilation

Pulmonary ventilation is expressed as liters of air expired per minute, the volume of gas being reduced to the standard temperature and pressure 0°C and 760 mm Hg, dry. The formula is

$$\frac{P_B - P_{H_2O}}{760(1 + 0.00367T)} \tag{1-1}$$

where P_B = ambient barometric pressure
P_{H_2O} = the vapor tension of water, mm Hg, at the temperature of the gasometer
T = the temperature of the gasometer, °C

To simplify this computation, one may use the line chart devised by R. C. Darling (Fig. 1-1). For routine calculations, use the large chart at the back of the book.

Respiratory Exchange Ratio or Respiratory Quotient (RQ)

The RQ is defined as the volume ratio of carbon dioxide production and the oxygen consumption, i.e.,

$$\frac{CO_2 \text{ production}}{O_2 \text{ consumption}} \tag{1-2}$$

and is utilized in the following calculations:

"True Oxygen," "True Carbon Dioxide," and RQ. The "true oxygen" represents the number of milliliters of oxygen consumed for every 100 ml of air expired. It is based on the following considerations: One desires to know the quantity of oxygen that is removed from the inspired air, but the only measurements made are the volume of air expired and its oxygen, carbon dioxide, and nitrogen content. The volume of inspired air usually does not have the same composition as that of expired air. This is because the RQ has to be exactly 1.00 for inspired to equal expired air. If the RQ is less than 1.00, as is usually the case in rest or moderate exercise, then the oxygen removed from inspired air is only partially replaced by carbon dioxide; and if 1 liter has been inspired, less than 1 liter will be expired. The nitrogen concentration in this case will be higher in expired than in inspired air. The concentration of nitrogen and other inert gas in outdoor air is 79.04 per cent, and the concentration in the expired air is determined by analysis on the Haldane apparatus. The volume of inspired air may then be calculated from the expired air by the formula

$$V \text{ inspired} = V \text{ expired} \times \frac{\%N_2 \text{ in expired air}}{79.04} \tag{1-3}$$

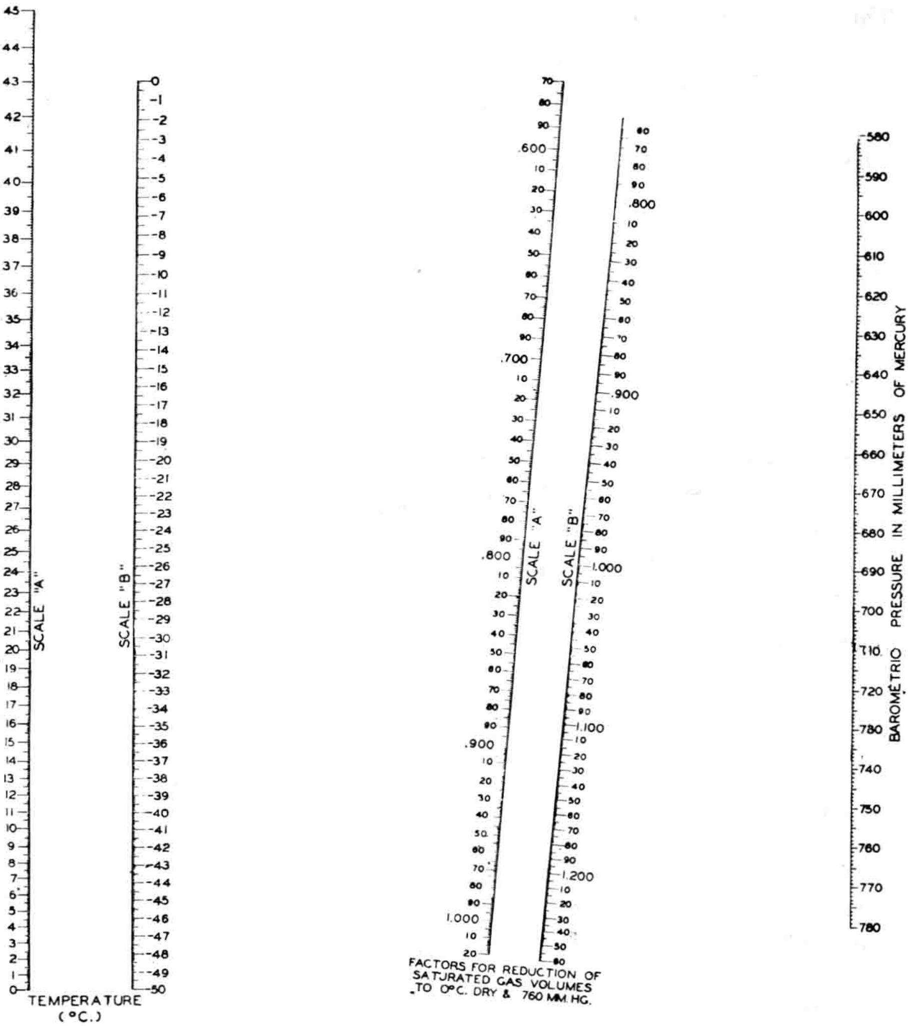

Fig. 1-1. Line chart for determining factors to reduce saturated gas volumes to dry volumes at 0°C and 760 mm Hg. This figure is an example of a nomogram. For laboratory use, the large, loose nomogram in the back of the book is recommended. (*Chart prepared by Robert C. Darling.*)

The total volume of oxygen inspired (not all consumed) is then

$$V_{O_2} \text{ inspired} = V \text{ air inspired} \times \frac{\%O_2 \text{ of inspired air}}{100} \qquad (1\text{-}4)$$

The percentage of oxygen in outdoor air is 20.93; hence,

$$V_{O_2} \text{ inspired} = V \text{ air inspired} \times \frac{20.93}{100} \qquad (1\text{-}5)$$

The volume of oxygen expired (amount not consumed) is

$$V_{O_2} \text{ expired} = \frac{\%O_2 \text{ in expired air}}{100} \times V \text{ air expired} \qquad (1\text{-}6)$$

The amount of oxygen consumed is

$$V_{O_2} \text{ consumed} = V_{O_2} \text{ inspired} - V_{O_2} \text{ expired} \qquad (1\text{-}7)$$

Substituting values from Eqs. (1-5) and (1-6),

$$V_{O_2} \text{ consumed} = V \text{ air inspired} \times \frac{20.93}{100} - V \text{ air expired} \times \frac{\%O_2 \text{ in expired air}}{100}$$

Substituting values from Eq. (1-3),

$$V_{O_2} \text{ consumed} = V \text{ air expired} \times \frac{\%N_2 \text{ in expired air}}{79.04} \times \frac{20.93}{100} - V \text{ air expired} \times \frac{\%O_2 \text{ in expired air}}{100}$$

Simplifying,

$$V_{O_2} \text{ consumed} = \frac{V \text{ air expired}}{100} (\%N_2 \text{ in expired air} \times 0.265 - \%O_2 \text{ in expired air}) \qquad (1\text{-}8)$$

The factor ($\%N_2$ in expired air $\times$ 0.265 $-$ $\%O_2$ in expired air) is the true oxygen, the number by which the volume of expired air (divided by 100) is multiplied to give the oxygen consumption (Fig. 1-2). Using a formula similar to that for the derivation of oxygen consumption, the carbon dioxide expired becomes

$$V_{CO_2} \text{ expired} = \frac{V \text{ air expired}}{100} \times \left(\%CO_2 \text{ in expired air} - \frac{\%N_2 \text{ in expired air}}{79.04} \times \%CO_2 \text{ in inspired air}\right) \qquad (1\text{-}9)$$

When one uses outdoor air, this becomes

$$V_{CO_2} \text{ expired} = \frac{V \text{ air expired}}{100} (\%CO_2 \text{ in expired air} - 0.03) \qquad (1\text{-}10)$$

The factor ($\%CO_2$ in expired air $-$ 0.03) is the true carbon dioxide, the number by which the volume of expired air (divided by 100) is multiplied to give the carbon dioxide production.

The respiratory exchange ratio (RQ) is obtained by dividing Eq. (1-7) by Eq. (1-6) and is

$$RQ = \frac{\%CO_2 \text{ in expired air} - 0.03}{\%N_2 \text{ in expired air} \times 0.265 - \%O_2 \text{ in expired air}} \quad (1\text{-}11)$$

To facilitate the computation of true O_2 and RQ a line chart was constructed [Dill and Fölling (1928)]. A piece of string stretched between the $\%O_2$ and $\%CO_2$ in expired air passes across these lines giving the RQ and "true O_2" directly (Fig. 1-2). For routine calculations, use the large chart at the back of the book.

Oxygen Consumption and Carbon Dioxide Production

The oxygen consumption in liters per minute is expressed as

$$\dot{V}_{O_2} \text{ (liters/min)} = \frac{\dot{V} \text{ gas (liters/min)}}{100} \times \text{true } O_2 \quad (1\text{-}12)$$

The carbon dioxide production in liters per minute is expressed as

$$\dot{V}_{CO_2} \text{ (liters/min)} = \frac{\dot{V} \text{ gas (liters/min)}}{100} \times \text{true } CO_2 \quad (1\text{-}13)$$

Energy Expenditure

It is conventional to express the metabolic cost of a given task in terms of kilocalories per hour. The large Calorie or kilocalorie is the amount of heat that is necessary to raise the temperature of 1 kg water 1°C, and it is the basic unit of all nutritional energy calculations. To compute the cost of a given task, the following formula is utilized:

$$\begin{aligned} \text{kcal/hr} &= O_2 \text{ consumption (liters/min)} \times 60 \times 5.0 \\ &= O_2 \text{ (liters/min)} \times 300 \quad (1\text{-}14) \end{aligned}$$

The factor 5.0 is an average value representing the calorie equivalent of 1 liter of oxygen consumed during moderate activity.

Since most common forms of work require an expenditure of energy which is directly proportional to the body weight, most tables of metabolic costs of activity are expressed on the basis of a standard man weighing 150 lb or 68 kg. To compensate for variations in weight, energy expenditure in work may be expressed in terms of Calories per hour and kilograms of body weight or converted to a standard body weight as follows:

$$\begin{aligned} \text{kcal/hr (standard man)} &= O_2 \text{ (liters/min)} \times 300 \\ &\times \frac{150}{\text{body weight (lb)}} \quad (1\text{-}15) \end{aligned}$$

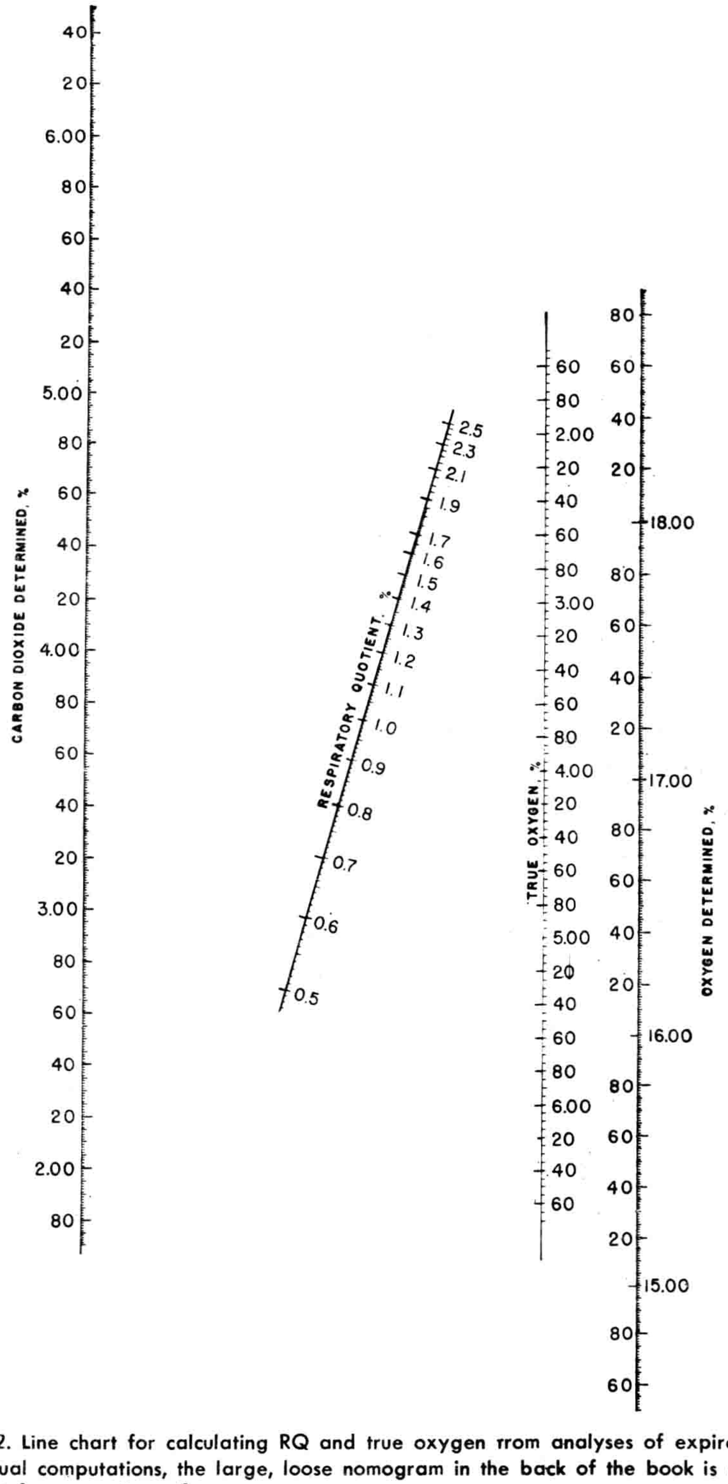

Fig. 1-2. Line chart for calculating RQ and true oxygen rrom analyses of expired air. For actual computations, the large, loose nomogram in the back of the book is recommended. [*Dill et al.* (1928)].

For some special purposes energy expenditure is computed on the basis of body surface area, not body weight alone. This will be discussed in the section on basal metabolism.

Example of Metabolic Calculations for a Walking Man (Using the Douglas Bag)

Subject marched 3.5 miles in 50 min on the level.
Weight of subject, stripped = 145 lb
Weight of clothes, helmet, pack, rifle, and canteen = 29 lb
Weight of metabolic apparatus = 13 lb

Douglas Bag Calculations

Collection started: 7 hr 30 min 0 sec
Collection ended: 7 hr 37 min = 7 min 0 sec
Gasmeter reading at the beginning = 448.0 liters
Gasmeter reading at the end = 662.9 liters, or a difference of 214.9 liters
Temperature = 21.9°C   Barometric reading = 757 mm Hg
STPD factor (from Fig. 1-1) = 0.880

$$\dot{V}\text{ (liters/min) STPD} = \frac{214.9}{7.00} \times 0.880 = 27.0$$

Haldane gas analysis: $\%CO_2 = 3.81$ $\%O_2 = 16.80$
Calculation of $\dot{V}_{O_2}$ from line chart for true O_2 (see Fig. 1-2).

$$\dot{V}_{O_2}\text{ (liters/min)} = \frac{\dot{V}}{100} \times \text{true } O_2 = \frac{27.0}{100} \times 4.23 = 1.14$$

$$\dot{V}_{CO_2}\text{ (liters/min)} = \frac{\dot{V}}{100} \times \text{true } CO_2 = \frac{27.0}{100} \times (3.81 - 0.03) = 1.02$$

Calculation of Energy Expenditure

kcal/min = O_2 (used liters/min) × 5 = 1.14 × 5 = 5.7
kcal/50 min = 5.7 × 50 = 285
kcal for 10-min rest (assumed) = 20
Energy expended in 1 hr that consists of marching 3.5 miles in 50 min *and 10 min rest* = 285 + 20 = 305 kcal.

Protein Metabolism During Work

The above calculations and examples neglect two factors which are not important in field measurements but which are theoretically important. Some of the calories are derived from protein, and 1 liter of oxygen consumed represents different amounts of heat depending on the ratio of fat, carbohydrate, and protein being consumed by the body at the time of measurement. Protein metabolism is determined from the **urinary nitro-**