BASAL METABOLISM

ITS DETERMINATION AND APPLICATION

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FRANK B. SANBORN, M.S., Editor

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"Health and good estate of body are above all gold, and a strong body above infinite wealth."

To THE MEN AND WOMEN
WHO APPLY SCIENCE IN DIAGNOSIS
AND
DILIGENTLY LABOR TO PREVENT
THE ADVANCE OF DISEASE

PENNSYLVANIA HOSPITAL, 8TH AND SPRUCE STREETS, PHILADELPHIA, PENNSYLVANIA.

The illustration shows the original building, the east wing of which was built in 1755. It was founded in 1751 and for the first four years occupied merely a dwelling house. Benjamin Franklin was largely instrumental in founding this, the oldest, hospital in America.

FRONT VIEW

The buildings from left to right are: Superintendent's Cottage, Medical Pavilions, Administration Building, Surgical Building.

LOS ANGELES COUNTY HOSPITAL, LOS ANGELES, CALIFORNIA

Representative of a modern public hospital that has been expanded and developt to meet the needs of a rapidly-growing American city.

REAR VIEW

From left to right: Tuberculosis Pavilion; Service Building; Power Plant; Laundry; Medical Pavilions; Garage and Morgue; Contagious Disease Pavilions; Psychopathic Ward.

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PREFACE

THIS book is intended to supply the physician and the technician with a treatise that will be a guide in making tests of metabolism and in interpreting the results of these tests.

No longer is it possible for a single individual, or a small group of individuals, to have a comprehensive knowledge of the various forms of apparatus and different methods of interpreting results that have developt in this rapidly-expanding subject of Basal Metabolism. This volume presents the judgments of many competent authorities. It is the product of many minds.

Ten chapters contain original articles. Each chapter has been prepared by a contributor whose views have been exprest without material curtailment, or regulation by the Editor or the Publishers. The Authors of the chapters on Determination of Metabolism were asked to make each chapter that describes a particular make or form of apparatus a scientific treatment and without criticism of other forms of apparatus, or methods. The Editor believes that this spirit of impartiality has been adhered to thruout the book. Nine forms of metabolism apparatus are described and information given of the best methods of using each apparatus so as to obtain the best results.

The chapters that contain methods of Application embody the views and opinions of the physicians whose names appear on the chapters.

Twelve chapters comprise abstracts which the Editor and his staff have prepared from important papers of recent date. These abstracts were submitted to the Authors and received their approval before being published in this volume.

The chapters that have not an Author's name affixt have been prepared under the direction of the Editor. He is responsible for these chapters as well as for the grouping, headings, and cuts in many of the remaining chapters. Miss Esther G. Price, A. B., collected and arranged most of the material in Chapters 1 and 2 on Normals. Miss Ruth A. Sanborn, B. S., has examined and made suggestions for many parts of the book, and prepared most of Chapter 27: A Conspectus of Recent Advances in Metabolism. Miss Mary A. Ruggles and Mr. V. R. Peterson, B. M. E., have collected and correlated many parts and read and checked both manuscript and text.

FRANK B. SANBORN.

BOSTON, MASS., U. S. A.

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TABLE OF CONTENTS

CONTENTS

NORMAL STANDARDS

INITIAL PROCEDURE
FOR ALL TYPES OF APPARATUS

OPEN CIRCUIT METHODS

Description — Procedure — Calculation

CLOSED CIRCUIT METHODS

Description — Procedure — Calculation

CLINICAL APPLICATIONS

IN GENERAL

IN HYPERTHYROIDISM

IN HYPOTHYROIDISM

IN FEVER

IN SURGERY

APPENDIX

DEFINITIONS

OF IMPORTANT TERMS IN METABOLISM TECHNIC

A-nab′o-lism.—The process of food assimilation; constructive metabolism.

Ba′sal Me-tab′o-lism.—The metabolism under basal conditions — after 14 hours of fasting and 12 hours of muscular repose — and unaffected by physical or mental exertion, or extraneous disturbance.

Ba′sal Met″a-bol′ic Rate.—The percentage that the actual basal metabolism is above or below the normal standard for an individual of the same sex, age, weight, and height.

Cal′i-brate.—To determine the caliber of; to establish graduations for an instrument, or to determine correct readings for a graduated instrument like a thermometer, or gasometer.

Cal″o-rif′ic Val′ue.—Number of calories generated when 1 liter of oxygen combines with a combustible to form heat. The calorific value of 1 liter of oxygen when protein is burned is 4.485; when fat is burned, 4.686; when carbohydrate is burned, 5.047.

Cal′o-ry, or Cal′o-rie.—The unit of quantity of heat is the small calorie, also called the gram calorie, written cal., the amount of heat required to raise one gram of water from 15° to 16°C.

Ca-tab′o-lism.—The series of changes by which living matter or protoplasm breaks down into less complex and more stable substances within a cell or organism; destructive metabolism.

Closed Cir′cuit Ap″pa-ra′tus.—Designating the type of metabolism apparatus in which a person rebreathes the gases in a gasometer.

Con-sump′tion of Ox′y-gen.—Volume of oxygen that is consumed and absorbed within the human system.

Di-rect′ Cal″o-rim′e-try.—The measurement of the heat eliminated by radiation and conduction together with the measurement of the heat eliminated by evaporation of water from the lungs and skin.

Gas-om′e-ter.—A tank for storing, mixing, or measuring gas.

In″di-rect′ Cal″o-rim′e-try.—Method of determining the respiratory exchange; that is, the oxygen that is consumed and the carbon dioxid exhaled by a person in a known time. From these 2 factors it is possible to calculate not only the heat production, but also to apportion the amount of oxygen that was used for the burning of protein, fat, and carbohydrate in the body.

Ky′mo-graf.—An instrument for recording various movements in the form of waves; used in metabolism tests to obtain grafic records of respirations.

Me-tab′o-lism.—The act or process by which, on the one hand, the food is assimilated into living matter — which is called anabolism or building up; and by which, on the other hand, living matter is broken down within a cell or organism into simpler products — called catabolism or tearing down. (Originally Metabolism was strictly an ecclesiastical term.)

Nor′mal Stand′ards.—The average basal metabolism for normal persons per unit of time: Normal Standards have been established from average results of extensive tests on normal persons.

O′pen Cir′cuit.—Designating the type of metabolism apparatus in which a subject inhales fresh air.

Re-sid′u-al Air.—The volume that is left in the lungs after a complete expiration.

Res″pi-ra′tion Cal″o-rim′e-ter.—An apparatus designed for the measurement of the gaseous exchange between a living organism and the atmosphere which surrounds it, and the simultaneous measurement of the quantity of heat produced by that organism. A complete respiration calorimeter, therefore, combines within one apparatus two separate and entirely distinct methods: the one determining the heat production and the other the heat elimination, thus allowing a comparison of the two principles.

Re-spir′a-tory Quo′tient. (R. Q.).—The ratio between the volume of carbon dioxid that is exhaled, and the volume of oxygen that is consumed in the same unit of time.

Re-spir′a-tory Rate.—The number of respirations per minute.

Spi-rom′e-ter.—An instrument for measuring the capacity of the lungs.

Stand′ard Pres′sure.—Pressure of the atmosphere at sea level; it is equivalent to a column of mercury that is 760 millimeters high.

Stand′ard Tem′per-a-ture.—Zero degrees Centigrade.

Ti′dal Air.—The volume that is given out during each respiration.

To′tal Ven″ti-la′tion.—Total volume of expired air.

BASAL METABOLISM

ITS DETERMINATION AND APPLICATION

CHAPTER 1

NORMAL STANDARDS OF BASAL METABOLISM

As the use of indirect calorimetry becomes more and more general as a routine aid to diagnosis in certain diseases, it becomes increasingly essential that accurate standards be available to clinicians by which they may judge of the normality or abnormality of the basal metabolism of their patients. It is, moreover, obviously desirable that in so far as possible, standards be uniform.

"Basal metabolism has been defined as the condition of minimal or fundamental exchange, the irreducible minimum of exchange of energy which is characteristic for the individual. It is the minimal activity of the body which maintains the functions of respiration, circulation, and secretion."[1] It may also be considered as "the sum total of all the vital activities of the quiet organism in the post-absorptive condition; i. e., the minimum of maintenance metabolism unaffected by extraneous factors. This may be expressed in terms of heat produced or of gaseous exchange incidental to heat production — carbon dioxid production and oxygen consumption. Using this basal metabolism as a standard, we may then measure definitely the superimposed factors."[2]

Normality of Subjects.— If standards are to be normal it is essential that the subjects used in establishing the standards be as near normal as is practicable. But one may well ask "What is normal?" Strictly speaking there is no such thing, because what is normal to one individual is not to another. Yet a person

[1] Lahey, F. H. and Jordan, S. M.: Basal Metabolism as an Index of Treatment in Diseases of the Thyroid — Boston Med. and Surg. Jour., **174**: 348-358, April, 1921.

[2] Benedict, F. G. and Talbot, F. B.: Metabolism and Growth from Birth to Puberty — Carnegie Inst., Washington, Pub. No. 302, 1921.

who is in good health and has no abnormal physical characteristic has been generally accepted as meeting the requirements of the case.

Uniformity of Conditions.— Granted that the subjects are normal, we must next be assured of uniform conditions in the tests from which the standards are to be computed; in every instance the *basal* metabolic rate must be obtained. This point cannot be too strongly emphasized if the normals that are established are to be truly normal; and only strict adherence to it will make it possible to make comparisons between the findings of different researchists, both at present and in the future — a comparison which is highly desirable.

Effect of Food, Posture, Sleep, Muscular Activity and Emotion.— The influence of all factors which are known to cause the metabolic rate to fluctuate should be eliminated during the tests. The effect of posture, food, sleep, mental anxiety or apprehension, and muscular activity must all be reckoned with. In the words of Roth "the test is for the determination of the *basal metabolic rate* and not the metabolic rate as influenced by apprehension, fear, fatigue, impatience, indignation, the tickling of a fly, discomfort, pain, or anything which increases muscular tension."[3]

It has been found that the metabolic rate in the sitting posture is higher than that in the reclining posture. Food in the stomach also raises the metabolism, and so in establishing normal rates it has been necessary, as in clinical tests, to have the patient in the post-absorptive condition. "The basal metabolism is always measured fourteen hours or more after the last meal, because food stimulates the heat production. A meal containing 60 grams of protein can increase the metabolism 10 or 12% for 6 or 7 hours. 100 grams of glucose may cause as great a rise, but for a shorter period. The stimulation from fat takes place much more slowly and does not reach its maximum until 6 hours after the meal. This stimulation caused by food is the specific dynamic action described by Rubner and studied in detail in the last few years by Lusk at the Cornell Medical College, New York City."[4]

[3] Roth, P.: Clinical Observations with Benedict's New Portable Respiration Apparatus — Boston Med. and Surg. Jour., **184**: 222-230, March, 1921.

[4] Du Bois, E. F.: Basal Energy Requirement of Man — Jour. Wash. Acad. Sc., **6**: 347-357, June, 1916.

The effect of sleep is slightly to lower the metabolism and in order that the accumulated tests may be strictly comparable it is advisable that all subjects be awake while tests are being made to establish normal standards. Any emotional disturbance, particularly fear and apprehension, will increase the metabolic rate and it is very important that such disturbances be obviated.

"Muscular work affects metabolism to a far greater extent than all other factors combined. Even walking at a moderate gait may increase the energy consumption threefold, and riding on a bicycle ergostat may increase it sixfold."[5] During severe, exhausting muscular work, almost at the limit of human endurance, the metabolism may be increased from 700 to 800 per cent.

Bearing all these facts in mind in his endeavor to conduct uniform tests on normal subjects, still further problems await the researchist who would establish normal standards. When the basal metabolism of an individual has been determined, shall it be considered in relation to his height, weight, body surface, or age?

Relationship Between Age and Standards.— One would expect age to have a definite bearing on metabolism, and research has proved this to be true. "The level of the metabolism varies greatly with age. During the first few days of life it is very low, then rises rapidly during infancy, and reaches its highest level in the almost unexplored period between the ages of 2 and 6 years. After this it falls rapidly until about the 18th year when the curve flattens out. Between the ages of 20 and 40 there is comparatively little change; but after this a slight fall, so that by the eightieth year the line is about 10 per cent. below the average level for the ages of 20 to 40. There seems to be a stimulation to the basal metabolism during the period of growth."[4]

Body Surface and Metabolism.— The search for suitable standards has centered chiefly about the so-called body-surface law of Rubner who was the first to appreciate the relationship between metabolism and surface area. "Of course the heat production of a man depends largely on his size, but it is by no means proportional to the body weight. A large man gives off more heat than a small man; but for each kilogram of weight the small person has the higher metabolism. On the other hand the

[5] Means, J. H. and Woodwell, M. N.: Remarks on Standards of Normal Basal Metabolism—Archiv. Int. Med., **27**: 608-619, May, 1921.

metabolism of men of various sizes and shapes is rather closely proportional to the surface area of the body. Many years ago Rubner established this law of surface area and was able to show that mice, rabbits, dogs, men, and horses had almost the same metabolism per square meter of skin."[4] The principle embodied in this law is that the basal metabolism is a simple function of the body surface. Even after the establishment of this principle, however, investigators were handicapt for years thru lack of an accurate method for measuring or calculating body surface.

The formulas of Meeh and Lissauer, that determine body surface from body weight, are fairly accurate for persons of normal proportions. But for those who are tall and thin, or short and fat, it has been found that there is a considerable discrepancy between the actual area and the calculated area; this discrepancy at times amounts to 16 per cent.

In 1914 Eugene F. Du Bois,[6] in collaboration with Delafield Du Bois, devised the so-called linear formula in which the body surface is computed from 19 measurements of the body. Casts were made of the bodies of 10 individuals who varied widely in form. "It was found that the area as calculated by the linear formula varied on an average less than 1.7 per cent. from the areas as actually measured from the casts. It was with the advent of this formula that calorimetry became available to the clinician. In the linear formula, the clinical investigator is equipt with a method that will give him accurately the surface area of individuals of any shape."[5]

"In 1916 the Du Boises brought out a still simpler formula: the so-called height-weight formula. This was worked out from the results obtained in a large series of persons by the linear formula, and enables one to obtain the surface area directly from the height and weight."[5] The height-weight formula is exprest in the terms $A = W^{0.425} \times H^{0.725} \times 71.84$; A representing the surface area in square centimeters; W, the weight in kilograms; H, the height in centimeters; and 71.84 being a constant. By this formula Du Bois was able to calculate the true surface area within an average error of plus or minus 1.5 per cent. and a maximal variation of plus or minus 5 per cent. From this formula a chart has been plotted, as shown on page 245, which

[6] Gephart, F. C. and Du Bois, E. F.: The Basal Metabolism of Normal Adults with Special Reference to Surface Area — Arch. Int. Med., **17**: 902-914, June, 1916.

makes it possible quickly to obtain the surface area of any individual whose height and weight are known. For very stout persons, however, it is still considered more accurate to use the linear formula.

The criticism that there is no casual relationship between body-surface area and the metabolic rate has been brought forward by Benedict. Lusk meets this criticism in the following manner: "I believe that the Du Bois standards for basal metabolism can be relied upon, and I also believe that, tho one may doubt the casual relationship between surface area and heat elimination, such doubt will not invalidate the arithmetic employed in the calculation. In making this statement I recall the words of Carl Voit, uttered regarding another matter:

"'I maintain this as an incontestable fact. It is so important that I question whether it is desirable to add a word of explanation. The results of a properly conducted and properly appreciated experiment can never be annulled, whereas a theory can change with the progress of science.'

"The establishment of a predictable basal metabolism enabled those working with the Russell Sage calorimeter to interpret the variations from the normal in many diseased conditions and has offered a method now widely accepted thruout the world for a closer clinical diagnosis of several pathologic conditions."[7]

Having this formula to compute the body surface, the next step was the "establishment of accurate standards with which to compare the heat production in hyperthyroidism, for example, with the heat which the patient would presumably have produced had he been perfectly well."[7]

Normal Standards for Adults.— Several well-known researchists — notably Du Bois, Benedict, and Dreyer — have endeavored to establish normal standards with which to compare the basal metabolic rate in any individual pathologic case. Eugene F. Du Bois considered body-surface and age the most accurate physiological factors to which to refer the metabolic rate of individuals. After the Du Bois formula for computing body surface had been devised — a formula which is simple and much more accurate than the formulas of earlier researchists — he continued a series of tests on normals, and with the collaboration

[7] Lusk, G.: Fundamental Ideas Regarding Basal Metabolism — Jour. Am. Med. Ass., **77**: 250-252, July, 1921.

of F. C. Gephart, published in 1916 a paper on "The Basal Metabolism of Normal Adults with Special Reference to Surface Area."[6] In this paper the authors state that the average metabolism of fat and thin subjects is the same according to surface area when the surface area is correctly measured. Tentative normal standards were presented at that time but were later revised.

Because of the paucity of data on the basal metabolism in old age, Aub and Du Bois undertook further study of basal metabolism of old men. It not being possible to find suitable subjects between 90 and 100 years of age, the age limits were reduced to between 75 and 85 years. Six men were obtained who fulfilled the requirements. Considering their ages they were in good health though they suffered from some of the pathologic conditions "which 'normally' accompany advanced years."[8]

"The calorimeter findings on the group of old men can be compared directly with the findings on Boy Scouts and normal adults between the ages of 20 and 47. The experimental methods used with all of these subjects were the same in almost all particulars. There was, however, one difference between the groups which could not be avoided. The younger subjects were active men on liberal diets, and almost all of them came to the calorimeter room from their homes on the mornings of the experiments. The old men were beyond the working age; they had been on rather meager fare, and they were all kept in the metabolism ward for several days before the tests were made. All of these factors tend to decrease the total metabolism in the same manner in which cage life affects a dog. Still they are part and parcel of old age. It would be difficult to find hard working men of 80 on large diets, or normal men in the prime of life leading the existence of octogenarians."[8]

It was necessary to exclude the findings for one of the six men tested because of the too great deviation from the mean. "The average basal heat production of the five men between the ages of 77 and 83 was 35.1 calories per square meter per hour, which is about 12 per cent. below the average for men between the ages of 20 and 50. This depression in old age is about 7 per cent. less than had been assumed by one of us in a curve based on results

[8] Aub, J. C. and Du Bois, E. F.: The Basal Metabolism of Old Men — Arch. Int. Med. **19**: 823-831, May, 1917.

obtained by other investigators. As one might expect, the depression of metabolism is somewhat proportional to the degree of senility . . . The methods of direct and indirect calorimetry agreed closely and the respiratory quotients were all within normal limits."[8]

At the suggestion of Drs. Means and Boothby, Du Bois, after considering the new data accumulated since 1916, revised his normal values for adults and in his paper on "The Basal Metabolism of Old Men"[8] published a new table of normal standards for the ages 14 to 80.

CALORIES PER SQUARE METER OF BODY SURFACE PER HOUR
HEIGHT-WEIGHT FORMULA — DUBOIS

Age, Years	*Males*	*Females*
14-16	46.0	43.0
16-18	43.0	40.0
18-20	41.0	38.0
20-30	39.5	37.0
30-40	39.5	36.5
40-50	38.5	36.0
50-60	37.5	35.0
60-70	36.5	34.0
70-80	35.5	33.0

A further discussion of the normal values for individuals who are under 20 years of age will be found in the section on Normal Standards for the Age of Puberty.

Benedict and Harris assert that the metabolism or heat output of the human body even at rest does not depend on Newton's law of cooling and, therefore, is not proportional to the body surface. They maintain that in predicting basal metabolism, "biologically, the most rational, and practically, the most satisfactory standard is that secured by taking into account the body weight, stature, and age of the subject."[9] Each of these factors they believe has an independent influence upon metabolism. They have, therefore, after a series of tests on normals, prepared two sets of tables, one of which shows the factor for a given body weight; the other, the factor for a given stature and age. After a factor

[9] Harris, J. A. and Benedict, F. G.: A Biometric Study of Basal Metabolism in Man — Carnegie Inst., Washington Pub. No. 279, 1919.

is obtained from each table, the two are added together and the result is the normal total heat production of the individual per 24 hours.

EXAMPLE: For a man weighing 70.4 kilograms, 168 centimeters in height, and 42 years old, the weight factor is 1035 and the height-age factor is 557. The normal total metabolism is the sum of the two factors, or 1592 calories per 24 hours.

A recent edition of the Harris-Benedict tables of normal values for adults may be found in "Tables, Factors, and Formulas for Computing Respiratory Exchange and Biological Transformations of Energy," prepared by Thorne M. Carpenter and published by the Carnegie Institution of Washington in 1921. (Paper covered, 123 pages, price, $2.50).

Dreyer[10] has objected to the introduction of the standing height as a factor in the calculation of the surface area on the ground that it is not a physiologic measurement, and he regards the sitting height as a more normal expression. He has evolved a formula which is based on age and weight alone. He states that this formula indicates that basal metabolism is not a single function of body surface.

FORMULAS FOR PREDICTING BASAL METABOLISM OF MALES AND FEMALES (DREYER)

The formula for males is $C = \frac{\sqrt{W}}{0.1015 \times A^{0.1333}}$, where C equals total calories per 24 hours, W equals body weight in grams, and A equals age in years.

EXAMPLE: Subject, 65 kilograms, 32 years.

(1)	Logarithm of W (69000)	2)4.81291
(2)	$\sqrt{W}$	2.40646
(3)	$A \times 0.1333$	0.20064
(4)	0.1015	$\bar{1}.00647$
(5)	Sum of (3) and (4)	$\bar{1}.20711$
	Subtracting (5) from (2)	3.19935
	Calories per 24 hours	1583

The formula for females is $C = \frac{\sqrt{W}}{0.1125 \times A^{0.1333}}$

The terms and the method are the same as those used for males.

[10] Dreyer, G.: Normal Basal Metabolism in Man and Its Relation to the Size of the Body and Age. Exprest in simple Formulae—Lancet, **2**: 289-291, Aug. 1920.

Normal Range of Variation.— "There is a normal range of variation amounting to plus or minus 10 per cent. from the average, and a few apparently normal individuals may depart as much as 15 per cent. from the mean. Curiously enough very fat people and very thin ones have almost exactly the same heat production, measured in this way, while there may be a difference of 30 to 40 per cent. between the two groups if we base the calculation on kilograms of body weight . . . Women show an average basal metabolism about 7 per cent. lower than that of men of the same age. Athletes are about 7 per cent. higher than men of sedentary habits."[8]

"Nearly every woman, whether normal or abnormal, has a menstrual history suggestive of a heightened metabolic rate before her menstrual period. Frequently there is emotional instability, excessive nervousness, some sensation of heat and even slight increase in perspiration."[11] The possibility of a periodic rise or fall in the metabolic rate of women, due to the influence of menstruation, has therefore been raised.

Blunt and Dye have made 216 observations in the study of this question and reach no definite conclusion. In the 17 subjects studied they found considerable fluctuation during the menstrual period; but this fluctuation was so irregular, bearing no apparent relation to the beginning or end of the period, and in several cases being no greater than the daily fluctuation found in many individuals during the intermenstrual period, that they consider it doubtful whether menstruation has any appreciable effect upon metabolism.

Rowe,[11] on the other hand, finds a rather definite relationship between changes in the metabolic rate of women and the menstrual period. He refers to a previous research by Snell, Ford, and Rowntree[12] in which they find that "a rather constant rise occurs during menstruation or in the pre-menstrual period, the rise being followed by a post-menstrual fall." Of the 10 cases studied by them, 2 showed "practically constant rises and 6, constant rises varying from 4 per cent. to 14 per cent., the average being 10 per cent., while in 2 a drop in rate was encountered. Values outside normal limits, ± 10 per cent., were infrequent."

[11] Rowe, A. H.: Monthly Fluctuations in the Normal Metabolic Rate of Men and Women — Cal. State Med. Jour., Aug., 1921.

[12] Snell, A. M., Ford, F., and Rowntree, L. G.: Studies in Basal Metabolism — Jour. Am. Med. Ass., **76**: 515-523, Aug., 1920.

Rowe's study of the effect of menstruation on the metabolic rate of women up to the present time has been made with the modified Tissot apparatus on 6 subjects. His charts show "first, a uniform pre-menstrual rise occurring within the week preceding the onset of the period . . . ; secondly, that with the onset of menstruation or possibly a few hours before, the metabolic rate probably falls and may reach its lowest level during the menstrual period or within the following two weeks. "The rates in the cases observed fluctuate up to a maximum of from 13 to 18 points.

"That menstruation influences the metabolic rates of women, therefore, seems quite probable. We feel that this menstrual influence should be recognized and taken into account in the establishing of a normal standard for women . . . Moreover, clinically, it is important for us to realize that the metabolic rate varies according to the menstrual cycles. No rate of a woman should be quoted without a record of the probable pre-menstrual and post-menstrual intervals. It is interesting to note that literature contains records of hyperthyroidism which is present only at menstruation. Such cases might have a post-menstrual rate of + 8 per cent. to + 12 per cent. and pre-menstrual rate of + 20 per cent to + 30 per cent., and unless the symptomatology were definite the diagnosis might be missed if only the post-menstrual rate were taken. A hypothyroid case might likewise be overlooked if a premenstrual rate of — 14 per cent. to — 10 per cent. were obtained. Of course the clinical manifestations are in all cases of the greatest importance."[11] From his rather limited observations Rowe concludes that "the menstrual cycle produces a definite metabolic curve in woman, the highest point being in the pre-menstrual week."[11]

Relative Merits of Normal Standards.— The Du Bois height-weight chart with the Sage Institute standards has been very widely used for computing the normal metabolic rate for individuals. The Harris-Benedict and Dreyer values have also a large number of advocates and the clinical calorimetrist may well be in doubt as to which of these, the Du Bois, the Harris-Benedict, or the Dreyer, he should use.

Means and Woodwell,[5] in a recent article, have presented a critical analysis of the variations between, and the relative accuracy of, these three current standards for the normal rate of basal metabolism. After a thoro study of the merits of the three standards they reach the conclusion that "in one sense it is really of small consequence which method the clinical calorimetrist uses, since the results obtained with the three are so similar. Uniformity, however, is always advantageous and it is best not to abandon an old method for a new one unless the new presents some material advantage over the old. The Du Bois method is the one in common use today. Since neither the Harris-Benedict nor the Dreyer methods have made any material improvement on it we believe it wise to continue with it, and especially in view of the fact that the existence of calorimetry in the clinic today is due in large measure to the work of Du Bois."

Means and Woodwell in the same article suggest that a subtraction of 1.8 calories from each of the Du Bois standards as they appear in the paper on "The Metabolism of Old Men" will render the difference between the Du Bois and the Harris-Benedict values so slight as to be almost negligible. Such a means would seem to present the most probable values and afford the highest degree of accuracy which is possible until further tests have been made. Accordingly, the following table has been prepared, the use of which is recommended. (The values for ages below 20 are probably more subject to change after further experiments than are the values for ages above 20).

DU BOIS NORMAL STANDARDS OF BASAL METABOLISM WITH 1.8 CALORIES DEDUCTED

(HEIGHT-WEIGHT FORMULA)

	Calories per Square Meter per Hour	
Age, Years	*Males*	*Females*
14-16	44.2	41.2
16-18	41.2	38.2
18-20	39.2	36.2
20-30	37.7	35.2
30-40	37.7	34.7
40-50	36.7	34.2
50-60	35.7	33.2
60-70	34.7	32.2
70-80	33.7	31.2

Normal Standards for Children.—The most extensive research on the metabolism of children under 12 years of age, so far reported, is that made by Benedict and Talbot, the results of which appear in a recent publication entitled "Metabolism and Growth from Birth to Puberty."[2] In this research observations were made on 258 children from public and private schools and, in many instances, repeated observations were made on the same child in successive years. The research has been in progress nearly a decade. The general plan of study has been to make observations on the respiratory exchange of a large number of normal boys and girls that differ in age, height and weight and by a comparison of the average values thus obtained, to determine the influence of age, height, weight and sex upon the heat production, to derive normal standards, and to establish the requirements of basal energy.

Normality of Subjects. — For children as with adults in order to determine normal standards of basal metabolism the subjects should be normal. As to what factors govern the normal child it is customary to consider three factors: — height in relation to age, weight in relation to age, and height in relation to weight. In the past normality has been determined from height in relation to age or, frequently from weight in relation to age. Altho the relations of age and height, or age and weight, cannot be ignored it is believed by Benedict and Talbot that these relations are not as important as height to weight. That is, in normal boys and girls the relation of first importance is not what is the age and the height, nor what is the age and the weight, but rather what is the height and the weight? Furthermore not one alone — age, height, or weight — is a sufficient index to use in selecting normal boys and girls, but rather height and weight together are recommended.

After selecting a group of boys and girls who possess normal height and weight they may be classified as normal subjects and tests are then in order to determine normal standards of metabolism for these normal children. How shall the standards obtained from normals be exprest? In terms of age, body surface, or weight?

Normal Standards Referred to Age. — Benedict and Talbot found that when the metabolism of boys was referred to age and plotted in a chart, the points were widely scattered and there was "great irregularity in the grouping." The chart does, however, show a rapid rise in the total metabolism during the first year of life and, from the first to the thirteenth year, a somewhat slower but steady increase. The trend for girls from 2 to 4 years seems to vary considerably from that of boys. Age does not appear to have a sufficiently definite or uniform influence upon the metabolism of children to render it advisable to express the normal values in terms of age.

Normal Standards Referred to Body Surface.— When the total calories per 24 hours were referred to body surface and plotted on a chart, it was evident that the relationship between body surface and the metabolism of children was closer than the relationship between age and metabolism. In fact Benedict and Talbot feel that body surface affords a means of predicting the probable basal metabolism of a child with "reasonable accuracy" and that the total calories referred to body surface may be considered as distinctly helpful in indicating whether or not a given case has a great deviation from the general trend which is being tentatively established for children.

In computing the body surface Benedict and Talbot believe that the Du Bois linear formula may properly be applied to children weighing 6.27 kilograms or under, but emphasize the superior accuracy of the old Lissauer formula for computing the surface areas of young children, as does Du Bois also. They recommend the use of a modified formula for computing the body surface area of children:

$$\text{Area} = K \sqrt[3]{W^2}$$

In this formula W is the weight of the child in kilograms and K is a constant which varies with the weight of the child. There is also a slight difference in the constants suggested for boys and for girls as shown by the table:

CONSTANTS FOR USE IN FORMULA FOR COMPUTING BODY SURFACE AREA OF CHILDREN.*

Boys	*Constant*	*Girls*	*Constant*
Up to 6 kg.	10.0	Up to 6 kg.	10.1
6 to 15 kg.	10.6	6 to 10 kg.	10.6
15 to 25 kg.	11.2	10 to 20 kg.	10.8
25 to 40 kg.	11.5	20 to 40 kg.	11.1

* Prepared from Benedict and Talbot — Metabolism and Growth from Birth to Puberty.

Having computed the body surface of a child, and having determined his basal metabolism in cubic centimeters of oxygen per minute, it becomes necessary to compute the total calories produced by the child in 24 hours before comparing the figures with the curves on Benedict and Talbot's charts. No table, expressing the basal metabolism of children in terms of body surface, has been prepared since it was found that it was slightly more accurate to express it in terms of weight.

Weight the Determining Factor in the Metabolism of Children. Altho body-surface area affords a useful medium for expressing the normal standards of basal metabolism for children and is a more accurate index than age, Benedict and Talbot consider the weight factor to be most influential in determining the metabolism of a child, and their charts show that if the metabolism of children is referred to body weight the scatter of points is less. "With boys who have a body weight of 10 kilograms or above, more satisfactory results may be obtained in predicting the metabolism from a curve in which the calories are referred to surface." The same is true for girls.

It should be remembered that during the period of growth "the factors of age, weight, and stature are intimately correlated, very much more so than is the case with adults. Adults weighing 70 kg. are much more likely to vary in stature than boys of 30 kg. Similarly, adults weighing 70 kg. may vary in age from early youth to old age, while the variation in age of boys weighing 30 kg. will be very much less. It is thus probable that the body weights of boys automatically include the variations in age and stature. For practical purposes, therefore, and until the metabolism of children is given biometric analysis, the prediction of the total basal metabolism of boys 10 kg. and above may be made with a reasonable degree of accuracy directly from the curve based upon body weight . . . In every instance the prediction for boys is materially better than that for girls."

Therefore, since it seems evident that weight is the most reliable factor to which to refer the metabolism of children, as well as being a very convenient one, Benedict and Talbot have prepared a table "giving the most probable heat production for each half kilogram of body weight for both boys and girls. They are not intended to be used for children above 12 years of age." If the weight of a child is known, the physician may read directly from the table on page 239 the predicted basal metabolism for a child of this weight and compare it with the heat production actually measured to note if the measured values are abnormal.

It should of course be borne in mind that in physiology normal variations are so great as absolutely to preclude a mathematically established standard without deviations therefrom; and it is probable that variations within plus or minus 10 points in the metabolic rate may be considered as normal.

Strictly Basal Standards Difficult to Obtain with Young Children.— The necessity for having patients in the post-absorptive condition — without food for 14 hours prior to the test — plainly cannot be applied to infants or very young children. It has in fact been proved that with infants the increase in the metabolic rate due to food in the stomach is extremely small when compared with the increase due to the crying and restlessness which are attendant upon lack of food. Experiments on children under 2 years of age have, therefore, been run with food, and hence "the basal metabolism of children under 2 years of age can be compared with that of older children only on the distinct understanding that the values for the basal metabolism of the younger children are higher than they normally would be, owing to the influence of food."

With children from 2 to 6 or 7 years of age the element of restlessness is greater than with older subjects, so that the standards for children up to 7 years of age are not strictly comparable with those for adults. It is probable that all metabolism values established for children are higher than basal rather than lower than basal. However, the normal values established form a reliable basis for comparison with pathologic cases of the same age when tested under similar conditions.

Normal Standards for the Age of Puberty. — "During the later period of growth, from 12 to 17 years, one factor enters into the development of life which produces pronounced psychological as well as physiological alterations in the body, namely, the influence of puberty. . . . It is quite clear, therefore, that serious consideration of the influence of puberty upon the metabolism of young children is a necessary accompaniment of any extended study of the vital activities of youth."[13]

At present the age of puberty has not received sufficient attention to warrant the establishment of definite standards for

[13] Benedict, F. G. and Hendry, M. F.: The Energy Requirements of Girls from 12 to 17 Years of Age — Boston Med. and Surg. Jour. Vol. **184**, March and April, 1921.

basal metabolism, nor has it yet been determined how great an influence the establishment of puberty really has upon metabolism.

An interesting study of the basal metabolism of Girl Scouts between the ages of 12 and 17 years has recently been made by Benedict and Hendry.[13] They summarize their reasons for undertaking the research as follows: "Since the metabolism of girls has been considered experimentally very much less than that of boys, it seemed desirable, if possible, to begin our observations with girls. A second incentive for studying girls was the lack of connection between the curve indicating the trend of metabolism of girls from birth to 12 years of age and the general slope of the line indicating that of women."

The tests were made on groups of girls, not on individuals. Groups of 10 or 12 girls of nearly uniform age were selected from various troops of Girl Scouts. All the girls were selected on the basis that they were normal and in good health. It was difficult to avoid considerable variation in the height and weight of the individuals selected, but with the group system such variations play a relatively minor rôle. At the critical prepubertal and pubertal ages of 13 and 14 years groups were selected, as far as possible, in which the most decisive criterion of puberty in females, namely, menstruation, had or had not appeared. Each group received a light, uniform supper at the Carnegie Nutrition Laboratory and the girls engaged in no excessive muscular activity during the evening. Thruout the night they slept inside a respiration chamber and measurements of the carbon dioxid production were taken while they were in deep sleep. In this manner muscular repose and control of the factor of food ingestion were insured, and the computation of the probable heat production could therefore be made from the carbon dioxid output with a reasonably small error.

At 10 o'clock the girls prepared for bed, and at this time record was made of their nude weight and height. They then entered the respiration chamber. The subjects were instructed to be quiet and to go to sleep as soon as possible.

At the end of an hour ventilation was started, a sample of the residual air was taken for the calculation of the carbon dioxid in the chamber, and the first experimental period was begun. Periods of one half hour each were made from 11 p.m. to 2:30

a. m. They were then lengthened to an hour, and on the nights when the respiratory quotient was determined all ventilation was shut down for another hour and a half to allow the residual carbon dioxid to accumulate. Determination of the total carbon dioxid production during these periods with no ventilation was always made by analysis. During the last hour the ventilation was again started and the usual procedure followed. At 6:30 a. m. the cover of the respiration chamber was opened, the chamber rapidly ventilated with a high speed blower, and the resting pulse rate of each of the subjects was taken. After this the subjects were called, weighed carefully, and dismist.

From the data which was accumulated from the tests, determination of the actual minimum carbon dioxid production thruout the night was made; and since all the groups were studied under the same experimental conditions, we may compare the basal values that were determined for the different ages.

The respiratory quotients $\left(\frac{\text{vol. } CO_2}{\text{vol. } O_2}\right)$ for 4 of the 9 groups observed were 0.81, 0.81, 0.78, and 0.79. The investigators were considerably surprised at these low respiratory quotients which were found 7 or 8 hours after a meal of approximately 500 calories. Yet one can hardly question the accuracy of the Sondén apparatus for determining both carbon dioxid and oxygen, and all analyses were made by an experienced chemist. The deviations between the various quotients are so small as to justify the use of an average quotient, 0.79. From the practical standpoint this average quotient made it possible for the investigators to select the most accurate calorific value of carbon dioxid to be employed in the computation of the energy transformation. Accordingly, they used 3.086 calories as the calorific value of a gram of carbon dioxid and the heat production has been computed by multiplying the carbon dioxid by this factor.

The essential findings in this research may be summarized as follows:

The average basal heat production of groups of girls from 12 to 17 years of age was 1250 calories per individual for 24 hours.

The heat production per kilogram of body weight decreases regularly with increasing age from 29.9 calories for 24 hours at 12 years, to 21.7 calories at 17 years. The results indicate that the general metabolic trend is materially below the few scattered observations of earlier writers.

The heat production per square meter of body surface likewise decreases, but not so regularly, with increasing age, ranging from 928 calories for 24 hours at 14 years to 745 calories at 16 years.

The prediction for the heat production per unit of body weight appears to be somewhat more accurate than that per unit of surface area.

None of the results clearly prove any influence ot puberty, or of the prepubescent stage on the heat production.

BENEDICT-HENDRY NORMALS FOR GIRLS FROM 12 TO 17 YEARS PREPARED FROM TESTS ON GIRL SCOUTS

Age of Girls	*Calories per kilo. per 24 Hours*
12	30.9
12½	29.9
13	28.8
13½	27.7
14	26.7
14½	25.7
15	24.6
15½	23.6
16	22.6
16½	21.7
17	21.2

The conclusions which Benedict and Hendry draw, and the tentative normal standards of basal metabolism which they present for girls from 12 to 17 years of age are of distinct value as a basis of comparison for investigators who have the facilities for performing tests under similar conditions. Since the difference noted between the Benedict-Hendry standards and the Du Bois standards for girls of ages 12 to 17 is too great to be entirely accounted for by the difference in experimental conditions, it is evident that further investigation is necessary before we can know exactly what standards are normal for the age of puberty, and the extent to which the establishment of puberty influences basal metabolism.

Perhaps the most pronounced effect of approaching puberty upon metabolism is that reported for boys by Du Bois. He found a high specific metabolism with boys at the age of 12 and

13 years, while with the same boys 2 years later, after puberty was thoroly established, he found the metabolism was considerably lowered. He made observations on boys of 12 and 13 and, after an interval of 2 years, repeated observations on these boys, as well as making further observations on boys of 12 and 13. In reporting this second set of experiments, he makes the following statement. "Altho the majority of the boys come a little below the line that was drawn 2 years ago, the change is not great enough to make it advisable to draw a new curve. The important fact remains that there is a rapid fall in metabolism during adolesence. The average decrease for the 7 satisfactory cases studied is 13 per cent. Their average metabolism at the ages of 14 and 15 years is 44.1 calories per square meter per hour, which is 11 per cent. above the average for adult men between the ages of 20 and 40 years. In the 3 youngest boys the metabolism during the 12th year was actually greater in calories produced than during the 14th year, altho the boys showed a gain in weight of between 35 and 50 per cent."[14]

DU BOIS NORMAL STANDARDS FOR BOYS OF 12 TO 14 — TENTATIVE VALUES CALORIES PER SQUARE METER PER HOUR

Age in Years	*Calories*
12 to 13	50.7
14 to 15	44.1

Benedict and Talbot are at the present time studying the age of puberty in boys. From the limited data that has been obtained thus far they are inclined to disagree with Du Bois and they believe that, prior to puberty, there is no tendency for a change in the general trend of basal metabolism.

The foregoing discussion clearly demonstrates that the physician who attempts to compare the basal metabolism of pathologic cases between the ages of 12 and 19 with a definite normal standard will find it necessary to choose between the widely divergent values of Benedict and Hendry, and Du Bois, which have just been quoted. Pending further experiments, the continued use of the Du Bois normal values is recommended with the deduction of 1.8 calories, for the age of puberty, as for adults. These values are given on page 29.

[14] Olmstead, W. H., Barr, David P., and Du Bois, E. F.: Metabolism of Boys 12 and 14 Years Old — Arch. Int. Med. **21**: 621-626, May, 1918.

The Flexibility of Standards. The statement has been made that "there is no inflexible standard for normal metabolism for any given age, weight, height, and sex from which all normal individuals never vary."[15] This is of course true. "It would also be true if applied to other physiologic data of clinical value commonly determined, such as the temperature, the systolic and diastolic blood-pressure, the pulse rate, the acuity of hearing and vision, and the like."[16] It does not hinder us from using normal standards for temperature and blood pressure. Neither should it prevent us from using approximately normal standards for normal basal metabolism as a guide in the study of pathologic conditions. However, care in the interpretation of metabolic findings cannot be overemphasized and Benedict has sounded a fitting word of caution: "The interpretation of metabolism results is not a simple rule of thumb procedure. In fact, the interpretation of results now far exceeds in complexity the actual laboratory technic. The technical stumbling blocks to the advancement of metabolism studies in clinical medicine have, we believe, been overcome. The great intellectual stumbling block, namely, lack of education with regard to the significance of metabolism measurements, cannot be overcome by the efforts of any one laboratory, one school, or one teacher. Before using gaseous metabolism measurements, it behooves every physician to familiarize himself thoroly with the fundamentals of gaseous metabolism and its significance."[15]

Greater Uniformity and More Permanent Value in Future Experiments on Normals. — Talbot has made a plea for uniformity in the experimental conditions under which future researches on basal metabolism are conducted. This is in order that the results may be of greater and more permanent value. "It is the duty of 20th century experimenters to make experiments of more than passing value. Each experiment should contribute to our fundamental knowledge. Each year sees an increase in the significance of normal values; an effort therefore should be made to secure normal values which will be of service not simply in the current year, but for a decade. In other words, experi-

[15] Benedict, F. G.: The Measurement and Standards of Basal Metabolism — Jour. Am. Med. Ass. **77**; 247-250, July, 1921.

[13] Boothby, W. M. and Sandiford, I. S.: — Basal Metabolic Rate Determinations, W. B. Saunders, 1920.

ments on normals should serve not only their immediate purpose but should invariably contribute toward the sum of the knowledge of basal metabolism requirements of normal subjects."[2]

A brief summary of this chapter together with a full explanation of the method of computing the metabolic rate of individuals from the Du Bois, the Harris-Benedict, and the Dreyer standards will be found in the next chapter.

CHAPTER 2.

NORMAL STANDARDS AND METHODS OF COMPUTATIONS.

Fundamentals of Basal Metabolism.— It should be emphasized at this point that the correct computation of the metabolic rate is comparatively simple, whereas the correct interpretation and application of the results demands a thoro understanding of the fundamentals that underlie basal metabolism. A careful reading of Chapter 1 is, therefore, advised in order to obtain a knowledge of the importance of normal standards of basal metabolism, the fundamentals underlying their establishment, and the modes of procedure which have been followed in determining these normal standards. Before discussing the methods of computing the metabolic rates of individuals from the values which have been determined as normal standards of basal metabolism, it seems advisable to review briefly the salient points in the foregoing chapter.

Definition of Basal Metabolism.— Basal metabolism is the irreducible minimum of exchange of energy which is characteristic for the individual; the sum total of all the vital activities of the quiet organism in the post-absorptive condition. It may be exprest in terms of heat produced or of gaseous exchange incidental to heat production — carbon dioxid production and oxygen consumption.

Normal Standards of Basal Metabolism.— In establishing standards of basal metabolism which purport to be normal, care must be taken that the metabolic rate which is obtained is basal.

It may be true that basal metabolism is not strictly proportional to, nor determined by surface area, but it appears to be more nearly proportional to area than to any other factor so far discovered.

The standards for women are 7 per cent. lower than those for men, and it seems probable that in considering the metabolism of women the influence of menstruation should be considered.

In comparing the metabolism of a pathologic case with the normal rate, it must always be borne in mind that the standards are not inflexible.

The standards for adults, old age, and children may be considered as approximately accurate. The standards for the age of puberty are tentative only.

The Modified Du Bois Standards for Adults.—The normal standards as proposed by Du Bois, Benedict, and Dreyer each have unique merits, but it seems best, in the interests of uniformity, to continue to use the standards established by Du Bois with 1.8 calories deducted from each value for ten year periods since Means, after a thoro study of the merits of the three standards concludes that neither those of Benedict nor of Dreyer have made definite improvements over those of Du Bois. Lusk confirms this opinion. The Du Bois standards as modified by recent suggestions may be found in the table on page 29.

The Benedict-Talbot Standards for Children.—For children it seems best to use the standards recently established by Benedict and Talbot after 258 observations on children from one to twelve years of age. These values are given in the table on page 239.

Normal Standards for the Age of Puberty.—For the age of puberty the use of the modified Du Bois standards is recommended. See table on page 29. As has been emphasized in the foregoing chapter, the values for the age of puberty are merely tentative. Moreover, the different researches have not been conducted under similar conditions, nor have the results been referred to the same factors. Until the results of further researches have been reported and the relative merits of these findings have been determined, it would be misleading to plot a continuous curve for normal values from infancy to old age. For the same reason it is inadvisable to present a continuous table of values.

Methods of Computing Normal Basal Metabolism.—The following examples illustrate methods of computing normal basal metabolism for adults, children, and the age of puberty by the modified Du Bois standards, the Sanborn tables, and the Benedict-Hendry standards.

Computations of Normal Standards for Adults (20 to 80 years).— Case No. 1: Male; age, 25; height, 175 cm.; weight, 70 kg. The method is in brief to multiply the number of calories that are required for one square meter by the number of square meters in the body surface, thus to obtain the total calories, or normal basal metabolism of an individual. The calories required per hour per square meter are given in a table on page 25; for Case No. 1, 37.7 calories per square meter per hour.

To find the number of square meters in the body surface of Case No. 1, refer to the Du Bois height-weight chart, page 245; follow the vertical line representing 70 kg. and the horizontal line representing 175 cm. until they intersect; the surface area may be read at the point of intersection as approximately 1.84 square meters. The above is the common method of finding surface area.

A new method of finding surface area is presented by the table on page 246. Enter the table with the 175 cm. and 70 kg. of Case No. 1; the body surface is directly read as 1.85 square meters. This makes a simple and quick method of finding body surface area. The table has been computed by logarithms from the Du Bois height-weight formula.

After the body surface area has been determined, whether by reference to the chart or the table, multiply by the calories per square meter. For Case No. 1 it would be 37.7 × 1.85, or 69.74 calories per hour, as the normal basal metabolism.

Since by the indirect method the patient's metabolism is usually measured in cubic centimeters of oxygen per minute, it is necessary for purposes of comparison to convert the calories of heat per hour into cubic centimeters of oxygen per minute. This is accomplished by use of the formula

$$\frac{\text{cals. per hr.}}{4.83 \text{ (cals. per liter of oxygen)}} \times \frac{1000 \text{ (c. c. in a liter)}}{60 \text{ (min. in an hr.)}}$$
$$= \text{c. c. of oxygen consumption per minute.}$$

A table of oxygen consumption equivalents has been prepared from this formula for 30 calories to 90.5 calories inclusive. By turning to this table (page 237) it is possible to read directly from the calories, the cubic centimeters of oxygen consumption per minute. For Case No. 1, the oxygen consumption corresponding to 69.74 calories of heat poduction is found to be 241 c. c. per minute.

Computation for Children (1 to 12 years).— Case No. 2:— Sex, female; age, 10; height, 132 cm.; weight, 29 kg. To compute the normal basal metabolism of this case from the Benedict and Talbot standards (see page 239) we find 29 kg. in the weight column and select the corresponding figure in the column for calories per 24 hours for girls — 1020 calories. Again, by the table on page 237 the equivalent of 1020 calories is 147 c. c. per minute — the normal basal metabolism of Case No. 2.

Computation for the Age of Puberty (12 to 20 years).— Case No. 3:— Sex, male; age, 14; height, 148 cm.; weight, 40 kg. To compute the normal basal metabolism of this case by the modified Du Bois method, follow the procedure given for Case No. 1.

Case No. 4:— Sex, female; age, 17; height, 160 cm.; weight, 52 kg. The basal metabolism of this case may be computed in three ways, i. e., by the modified Du Bois standards, by the Sanborn tables, or by the Benedict-Hendry standards.

1. **By the Modified Du Bois Standards.**— Turning to the table on page 29, we find the normal heat production per hour per square meter of body surface for a girl of 16-18 years to be 38.2 calories. Determining the surface area from the height-weight table on page 246, we find it to be 1.52 square meters. Multiplying 38.2 calories by 1.52, we get 58.1 calories, the normal basal metabolism per hour for this patient. Next we turn to the table of equivalents (page 237) and find opposite 58.0 calories — 200 c. c., the normal consumption of oxygen per minute for Case 4.

2. **By the Sanborn Tables** (based on the modified Du Bois standards).— Case 4: Sex, female; age, 17; height, 160 cm.; weight, 52 kg. We find 52 kg. and 160 cm. on the table. By following down the column for 160 cm. to the point where the predictions for 52 kg. cross it, we find 196 c. c., the normal consumption of oxygen for a man of 20 of the same height and weight. Add 10 per cent. to obtain the basal metabolism of a boy of 17, and from this subtract 7 per cent. for sex, the final result being 201 c.c.

3. **By the Benedict-Hendry Standards.**— Case 4: Sex, female; age, 17; height, 160 cm.; weight, 52 kg. In the Benedict-Hendry table we find that the normal standard of heat pro-

duction for a girl of 17 is 21.2 cals. per 24 hours per kg. Therefore, since this patient's weight is 52 kg., her normal heat production per 24 hours will be 21.2 cals. $\times$ 52 = 1102 cals. per 24 hours, or 45.9 cals. per hour. Reduce this to c. c. of oxygen per minute (see page 237); and the normal consumption for Case No. 4 proves to be 159 c.c. per minute.

The wide difference between the results obtained by the Benedict-Hendry standards and those by the modified Du Bois standards (or by the Sanborn tables) has been previously discust in the Chapter 1, the section on "The Age of Puberty." Normal values for this Age have not been well established and further tests are now being made.

CHAPTER 3

PREPARATION OF PATIENT

By John Walker Moore, M. D.

Interpretation of "Basal."—The rate of metabolism of an individual, in health and in disease, is subject to marked physiological fluctuations. The physiological variations must be reduced to a minimum in order to establish a convenient basis for comparison of metabolism of different individuals, or of the same individual on different occasions. The term universally selected to designate this basis is known as Basal Metabolism, and may be defined as the minimum heat production of an organism at complete muscular rest and in a post-absorptive condition, or, as Harris and Benedict[1] have exprest it, the catabolism in the absence of muscular activity and the stimulating influences of recently ingested food. It must be borne in mind that the modern conception of basal metabolism does not mean the lowest possible metabolism, for Benedict has shown that the metabolism during sleep sinks to a lower level than when the patient is awake and in complete muscular repose.

Physiological Factors.— In order to prepare the patient so that the pathologic variations in metabolism can be correctly interpreted, it is essential to reduce to a minimum the fluctuations in metabolism that are physiologic in origin.

The two main physiologic factors that influence the rate of metabolism in man are: first, muscular activity; and second, the ingestion of food.

Muscular Activity.— Benedict[2] has shown that a trained athlete was capable of increasing his basal metabolism eight-fold by doing severe muscular exercise in form of bicycle riding, and that the metabolism was maintained at a high level for a considerable period after the cessation of work.

Zuntz[3] and his associates found that walking on a level at a

[1] Harris, J. A., and Benedict, F. G.: The Variation and Statistica Constants of Basal Metabolism in Men.— Journal Biol. Chem., **46**. 257-279 1921.

[2] Benedict, F. G., and Emmes, L. E.: A comparison of Basal Metabolisml of Normal Men and Women.— Journal Biol. Chem., **20**: 263-299, 1915.

[3] Hewlett, A. W., Pathological Physiology. Appleton, 1917.

moderate pace increased the metabolism about 3 times, while walking rapidly on a level increased the metabolism about 5 times above the basal value. In attempting to produce a condition similar to that present in patients coming from their homes to an office or hospital for basal metabolic rate determination, Snell et al.[4] found that immediately after walking 300 yards, or up 2 flights of stairs, the metabolic rate was increased on an average of 58 per cent. They conclude that these patients would revert to a basal condition in one-half to one hour, if allowed to rest.

Slow periodic raising and lowering of the arms, repeated 2 to 3 times per minute, or even the regular movements of the fingers have been demonstrated by Speck[5], Stuve[5] and others to raise the oxygen consumption 10 to 20 per cent. The work of mastication, such as would be involved in chewing gum continuously, may increase the heat production 17 per cent.

Muscular Activity — Result of Discomfort.— Emmes and Riche[6] found that the consumption of oxygen averaged 7.6 per cent. higher with the patient sitting upright in a chair with the head supported, than when lying flat in bed. Boothby and Sandiford,[7] using the gasometer method, found no constant variation in the metabolic rate when patient was either sitting in straight back chair or lying flat in bed. Of the 25 cases studied, 13 showed an average increase of 7 per cent., and 9 showed an average decrease of 5 per cent. when sitting, while 2 cases showed no change as the result of position. They believe the slight variation found to be due in all probability to a more complete muscular relaxation in one instance than in the other. Magnus-Levy[5] calls attention to the alterations of the body position as a whole, or of the limbs, or even an uncomfortable position which tends to keep muscles on the stretch, as causing a raise in the oxygen consumption 10 to 20 per cent. or higher. Soderstrom et al.[8] found the metabolism averages 3 per cent.

[4] Snell, A. M., Ford, F., and Rowntree, L. G.: Studies in Basal Metabolism. Jour. Am. Med. Ass., **75**: 516, 1920.

[5] Von Noorden's Metabolism and Practical Medicine, Vol. 1: The Physiology of Metabolism. Keener and Company, Chicago, 1907.

[6] Emmes, L. E., and Riche, J. A.: The Respiratory Exchange as Affected by Body Position.— Amer. Jour. Physiol. **27**: 406-413, 1910-11.

[7] Boothby, W. M., and Sandiford, Irene.: Laboratory Manual of the Technic of Basal Metabolic Rate Determination. Saunders, 1920.

[8] Soderstrom, G. F., Meyer, A. L., and Du Bois, E. F.:. Clinical Calorimetry Paper XI. A comparison of the Metabolism of Men Flat in Bed and sitting in a Steamer Chair.— Arch. Int. Med., **17**: 872, 1916.

lower with patients in the semi-reclining position than when lying flat at rest.

Other conditions that may produce an increase in the rate as the result of discomfort may be enumerated. The desire to urinate; this may be so urgent that the rate is increased 20 per cent., as was found in one of the writer's series; particularly is this true in cases of diabetes insipidus. Women with hair arranged in a knot in back of head often suffer discomfort as the result of pressure of hair pins. Tight fitting articles of dress, as corsets, collars, coats, etc., as well as strong lights so arranged that their rays shine directly in patient's eyes, all produce a measureable increase in metabolism. The discomfort that is frequently complained of by patients as the result of using ill-applied or ill-arranged breathing appliances is a factor that must constantly be borne in mind as a potential cause of increased oxygen consumption.

The extent to which ventilation or oxygen consumption returns to normal depends upon the amount of work done. A. Loewry[5] found the oxygen consumption returns to normal 4 to 9 minutes after medium work, and 20 minutes after fatiguing work. After severe work there was a slight rise after 20 minutes of rest. Benedict and Cathcart[9] report a case in which there was an increase in the basal metabolism for from 5 to 6 hours after the subject rode a bicycle for 70 minutes, doing work equivalent to 2.06 calories per minute. As has already been pointed out, Snell et al.[4] believe that the increased metabolism brought about by a patient coming to hospital or office for a metabolic rate determination becomes basal as the result of complete rest for one-half to one hour. Boothby and Sandiford's[7] conclusion, based upon much experimental data, is that 20 minutes is a sufficiently long rest to insure a basal condition, provided no strenuous exercise precedes the rest period.

Effect of Food.— Studies in metabolism have shown that there is liberation of heat after the ingestion of food and that this may last for 12 hours or more. The heat production is greater following the ingestion of protein than any other food stuff.

In man, according to Gephart and Du Bois[10], the ingestion

9 Lusk, G. Science of Nutrition, Philadelphia, Saunders, 3rd Edition, 1917.

10 Gephart, F. C., and Du Bois, E. F. Clinical Calorimetry, Paper IV. The Determination of the Basal Metabolism of Normal Men and the Effect of Food. Arch. Int. **15**: 835, 1915.

of 200 grams of glucose or 105 grams of nitrogen in form of casein increases the heat production about 12 per cent. over a period of from 3 to 6 hours. With a larger protein meal, consisting of 239 grams of nitrogen in the form of chopped beef and 100 grams of fat, these writers found the basal metabolism was much increased, showing a plus 26 per cent. at the end of 10 hours.

Lusk found the heat production in man increased 46 per cent. after the ingestion of a large protein meal, and the increase did not disappear for about 12 hours.

Soderstrom, Barr and Du Bois[11] studied the effects of a selected standard breakfast consisting of a slice of bread (20 grams), butter (8 grams), 200 c. c. of caffein-free coffee, containing 10 grams cane sugar and 60 c. c. of milk. This breakfast contained protein, 4.7 grams, fat, 9 grams, and carbohydrates 28.9 grams. They found that in the first hour following the ingestion of the food the average heat production was increased 7 per cent., in the second and third hours, 2 per cent., in the sixth and seventh the metabolism was slightly lower than basal. They believe a post-absorptive condition is reached 5 hours after the ingestion of the standard breakfast.

Lusk[9] points out that the increase in metabolism following the ingestion of glucose dissolved in cold water, is the result of the effort of the individual to provide for the body heat lost to the fluid in the stomach. This author cites from Tangl's laboratory the findings of greater metabolism in man after the ingestion of a liter of cold milk than after taking the same amount when warm. It has been shown that after the ingestion of 500 c. c. of water at 20° C., the original temperature of the stomach is not regained for from 70 to 75 minutes.

Miscellaneous Physiological Causes of Abnormal Oxygen Consumption.— Many patients, intelligent or otherwise, especially the latter, appearing for the first time to have their metabolic rate determined, are nervous and restless from apprehension. Though in most instances they desire fully to cooperate, still there remains a secret fear which prevents a basal condition.

11. Soderstrom, G. F., Barr, D. P., and Du Bois, E. F.: Clinical Calorimetry, Paper XXVI. The Effect of a Small Breakfast on Heat Production.—Arch. Int. Med. **21**: 613-620, 1918.

A cold bath, especially when taken before breakfast, causes a great increase in metabolism. Lusk[9] quoting Rubner's experiments, showed that a tub bath at 16°C., taken before breakfast, increased the oxygen consumption 46.8 per cent., whereas a douche at 16°C. increased the oxygen consumption 110.1 per cent. The metabolism remains increased for about one and one-half hours. This author states that a bath of 35°C. has no effect on metabolism.

It has been found that an imperceptible air current may have a profound influence upon metabolism. Rubner has shown that wind, having a velocity of 0.18 meter per second, acting upon the exposed area of the arm, increased the heat loss between 19 and 75 per cent. depending upon the temperature of the wind.

Snell et al.[4] found a rather constant rise in metabolism during menstruation, or in the premenstrual period, the rise being followed by a post-menstrual fall. The average rise in cases studied was 10 per cent.

In the early weeks of pregnancy, there is little or no increase of metabolism above the normal; however, in Baer's[12] series, the curve showed a gradual rise from a plus 26 per cent. in the thirty-fourth week to a plus 33 per cent. in the fortieth week. The rate became normal about the eleventh day of post-partum.

Benedict found, in fasting or otherwise, that there is a diurnal variation in metabolism amounting, in a fasting subject, to an increase of 14 per cent. of the morning metabolism and 22 per cent. in the late afternoon over the metabolism during sleep.

Smoking a cigarette up to within one and one-half hours of the test apparently has little effect upon metabolism. To determine the effect of smoking upon basal metabolism, six normal fourth year medical students were studied. In all the determinations, the subjects were allowed to smoke a cigarette one and one-half hours before the initial test. On the following morning the test was repeated without smoking. Four of the subjects smoked regularly, but not before breakfast. Their metabolic rates were increased after smoking on an average of 3.2 per cent. the highest being 5.9 per cent. One of the subjects had never acquired the habit, but usually smoked once or twice

12. Baer, J. L.: Basal Metabolism in Pregnancy and the Puerperium.—Am. Jour. of Obst. and Gynecology, **2**: 249-255, 1921.

a month; in his case the rate was increased 1.3 per cent. after smoking. The other subject had been an inveterate smoker up to 2 years ago, since that time he has refrained entirely from the use of tobacco. His normal metabolic rate was plus 2.6 per cent., after smoking it was minus 1 per cent. a decrease of 1.6 per cent. Altho this series is too small to draw definite conclusions, the evidence shows that a cigarette smoked in a limited time before the test has little effect upon metabolism.

Routine Preparation of Patients for Obtaining a Basal Condition.— In order to obviate false metabolic rates as the results of the physiological factors that have been pointed out in the above, we recommend the following routine procedure to be carried out on all patients to be tested:

1. Patient is told to refrain from violent or fatiguing muscular exertion the day before the test, and to retire not later than 10 o'clock that evening.

2. He is directed to eat a light supper, preferably without meat, not later than 7 o'clock the evening before the test; water but no food may be taken before bed time.

3. No breakfast, drugs, and preferably no water are to be taken the morning of the test, however a glass of moderately cold water, an hour and one half before the test, will probably not alter the rate.

4. A cold bath should not be taken on the morning of the test.

5. Smoking should not be permitted the morning of the test, unless the patient is in the habit of indulging before breakfast, and then, not within one and one half hours of the determination.

6. The patient should present himself at the metabolic station at 8 or 8:30 A. M. If in hospital, he should be brought in a rolling chair or on a litter; if ambulatory, he should refrain as far as possible from muscular exertion.

7. All stiff or constricting garments, as corsets, collar, belt, shoes, etc., should be removed, and women should take out all hair pins and combs. It is advisable that women should be provided with kimona.

8. Patient is directed to empty bladder, and also the bowels if necessary.

9. Patient is taken to metabolic room, which should be done

in cheerful but subdued colors with no unshaded lights; in addition, it should be well ventilated, altho without perceptible air currents, and the temperature maintained between 65 and 70° F.

10. The operators should be kind, sympathetic, and, above all, gentle. One of them should show the apparatus and explain the harmlessness of the test to the patient, assuring him that he is to breathe pure air or oxygen, and that an operator will be on hand during the entire test period.

11. Patient is put to bed lying on his back and is made as comfortable as possible with one or two pillows as desired; chewing gum, etc., removed from mouth.

12. If patient appears restless or apprehensive a preliminary test lasting from 3 to 4 minutes is carried out. The breathing appliance is then removed and the rest begun. He should be instructed that at no time is he to assist in adjusting the breathing appliance.

13. The rest period for hospital patients should be maintained for from 20 to 30 minutes; for ambulatory cases, 30 to 60 minutes, depending upon the extent of the previous muscular exertion. It is essential during this period to secure complete relaxation, and for this reason it is absolutely necessary to prevent anything that may tend to excite the patient, such as discomfort, noises, conversations, and friends or visitors. If the latter part of rest period is disturbed, as by movement, it should be extended 5 to 10 minutes longer, depending upon the degree of exertion.

14. To assure cooperation, and at the same time to allay any secret apprehension, with all patients a trial test should be carried out immediately before the actual test.

15. Temperature, pulse and respiration should be taken after patient is at rest in bed, but before the preliminary test. Pulse and respiration should be taken several minutes after this test, and again during the prelimimary and trial tests, as well as at 5 minute intervals during the actual test.

16. After the test has been completed the patient is weighed, nude, and height taken in bare or stocking feet.

All restlessness and nervousness, irregularity in breathing, swallowing, etc., should be carefully noted and recorded. Should the patient appear extremely restless, enough so as to cause a pathologic change in the basal metabolic rate, he should be told to come back for another test at some future date. This has the preference over attempting to secure a normal rate in a nervous individual by repeating the test in the same day.

CHAPTER 4

GAS ANALYSIS METHODS

Gas Analysis Methods[1] comprise the Zuntz-Geppert Apparatus that was developt in Germany about 1890; the Atwater Calorimeter, in America, just before 1900; the Tissot Gasometer, in France, about 1900; the Douglas Bag, in England, about 1910; and various modifications of the Tissot Gasometer that have been developt in America since 1900.

This chapter describes briefly the Douglas Bag Method, and the Gasometer Method, with special reference to details of Gas Analysis. The chapter that follows continues the Gas Analysis Method with special reference to the technic of the Gasometer that is used at the New York Post-Graduate Hospital; this technic is similar to that of the Mayo Clinic.

Douglas Bag Method.—This method is used principally in England. In America it has been used but very little. The method may be briefly explained by stating that the subject breathes fresh air and exhales into a rubber bag that serves as a container, or gas bag. The exhaled gas is measured in volume, usually by passing it out of the bag thru a meter; the component parts of oxygen and carbon dioxid are then determined by chemical analysis. The illustration shows the way the apparatus is arranged for demonstration. When a patient is reclining or lying in bed, the gas bag may be suspended from a hook on the wall, from a bed post, or from the back of a chair. The bag should have a free chance to expand.

The apparatus was developt by Dr. C. G. Douglas, and it was described by him in the Journal of Physiology, London, 1911. The subject breathes thru a mouthpiece or face mask that is connected with inspiratory and expiratory valves; fresh air enters thru the nose and the exhaled air passes out thru the mouth and into the bag, as shown by the arrangement in the cut.

[1] A Comparison of Methods for Determining the Respiratory Exchange of Man, by Thorne M. Carpenter, Carnegie Inst. of Washington, Pub. No. 216, 1915.

Or, by placing a nose clip on the nose, and thus preventing nasal respiration fresh air will enter thru the inspiratory valve which opens during a inspiration and automatically closes during expiration, when the expiratory valve will open to allow passage of the expired air into the bag. This principle likewise applies when a face mask is used: namely, the inspiratory valve opens only during inspiration, the expiratory valve only during expiration.

In connection with the Douglas Bag, there is usually a three-way valve which permits the subject to breathe into the open for a few minutes before the test, and into the bag during the test period of 10 or 15 minutes. The three-way valve is then closed and the apparatus removed from the patient. The rubber pipe is disconnected from the expiratory valve and attached to a gas meter. The gas is thoroly mixt by repeated pressure on the bag, the three-way valve opened and, while the volume of gas is being measured thru the meter, a sample of gas is taken off for analysis.

The Douglas Bag and the Gasometer Method, as described in the rest of this chapter and in the next chapter, both require some form of face mask or mouthpiece, inspiratory and expiratory valves, sampling tubes for gas, and a gas analysis apparatus.

Face Mask or Mouthpiece.— One form of face mask is shown by illustration in the next chapter. This mask covers the whole face. A half-mask that covers the nose and mouth only has heretofore been used by many technicians both in America and in Europe. A form of mouthpiece and of nose clip are illustrated in Chapter 12. It is difficult to tell positively whether or not leakage is occurring around a face mask, or a mouthpiece.

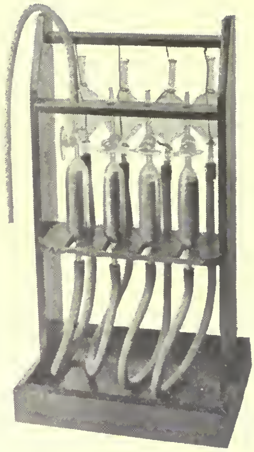
The patient can feel a current of cold air passing under a mask if there is undue leakage; or it may be observed by applying soap suds; or sometimes by listening closely.

Inspiratory and Expiratory Valves.— In gasometers, Douglas Bag or modified forms of apparatus, when the patient inhales, air enters thru the inspiratory valve, and when the patient exhales, air goes thru the expiratory valve into the gasometer or bag. These valves must open and close automatically and without leakage; they should be light weight so as to offer hardly any resistance to breathing; they should cause but a slight amount of noise, and it is most essential that no leakage occurs thru these valves when they are closed. The whole operation of these valves is a point for much emphasis. The valves as described by Dr. Tissot in Journal de Physiologie, 1911, were made of very thin brass, hinged on one edge. The valves have since been made with a mica seat. During the recent World War a very simple form of rubber valve was developt which at the present time is being more generally used than either the brass valves or mica valves.

Under average conditions rubber valves are satisfactory. If there is excessive moisture, however, or if the valves are used in high temperatures, they will stick. Many authorities believe that some form of valve should be devised which would be more nearly perfect than any hitherto developt.

Sampling Tubes.— Sampling tubes may be of the new form that is described by Dr. Bailey in the following chapter, or of the common laboratory form that is shown in the accompanying cut. The glass parts are usually shipt unassembled, and the illustration will serve as a guide for assembling. The glass parts are connected by rubber tubing which should have heavy walls, inside diameter of 3 mm. and be about 40 cm. long. A set of 4 tubes requires 5 of the above lengths of tubing, or about 200 cm. in all, and about 1800 grams (or 4 pounds) of mercury.

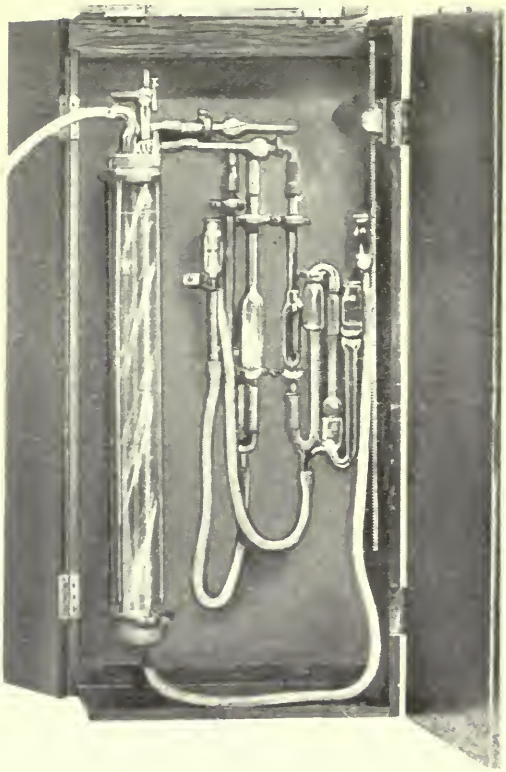
The process of collecting samples of the exhaled gas from the Douglas Bag or from the Tissot Gasometer is described in Haldane's small volume on "Methods of Air Analysis," and briefly



in Boothby and Sandiford's "Basal Metabolic Rate Determinations." Care should be taken (1) that the sample is not altered while it is being collected or afterwards while in storage; (2) that the sampling tubes, or container, be air-tight. After the rubber tubing from the sampling tubes has been connected to the Douglas Bag, or Gasometer, a sample of gas may be drawn into one tube by lowering the mercury reservoir with the pet cock open and closing the pet cock when the sample has been taken. The process should be repeated once or twice, thus to wash the sampling tube. A sample should represent the average quality or mean composition of the total amount that is in the Bag or Gasometer; for that reason, before taking the sample the gas in the Douglas Bag should be thoroly mixt. In the gasometer method one sample is usually taken with the gasometer at the top, a second midway, and a third when the gasometer is near the bottom; a fourth is sometimes taken. Four sampling tubes are usually filled as described above. Two tubes are analyzed for oxygen and carbon dioxid, and two are held in reserve.

The Haldane Gas Analysis Apparatus.—When assembled this apparatus corresponds to the illustration; when shipt an extra glass pet cock is left on the bottom of the buret. This pet cock may be used during calibration and afterwards broken off; usually there is a scratch around the glass tube where the break can easily be made, but if there is no scratch one may be made with a sharp, hard file.

The calibrations on the buret should be tested. They may be tested by filling the buret with mercury; drawing small portions, about 1 c. c. at a time, thru the extra glass pet cock into a weighed vessel, then computing the volume of these successive weighed portions and comparing with the graduations on the buret. The buret should be kept perpendicular, free of air bubbles; drops of mercury should be wiped off the end of the pet cock after each portion is drawn out; a constant room temperature should be maintained as 1 degree of change will cause an appreciable change of volume.



The process of analyzing samples of gas by the Haldane Method is explained in Haldane's "Methods of Air Analysis" and in Boothby and Sandiford's "Basal Metabolic Rate Determinations." The essential steps in the analysis are given in Chapter 5 of this book by Dr. Bailey: "In principle, a volume of air is drawn into a graduated buret where it is saturated with water vapor and measured; the air is then passed back and forth into a potash pipet where the carbon dioxid is removed; it is returned to the buret and again measured, the difference between this and the first reading representing the volume of carbon dioxid. The oxygen is removed in a similar manner by passing the air into a second pipet containing a potassium pyrogallate solution; after the oxygen is absorbed, the gas is returned to the buret and measured, this second loss in volume representing the oxygen in the sample of air."

The gas in one of the tubes that contains the sample is analyzed, a duplicate check being required upon the carbon dioxid and oxygen percentages.

The air that is breathed by a patient should not be room air, which varies in its component parts, but should be outside air which, according to Haldane, contains 20.93 per cent. of oxygen, 0.03 per cent. of carbon dioxid; and according to Boothby, 20.93 per cent. of oxygen, and 0.04 per cent. of carbon dioxid. The analysis usually comprises the determinations of oxygen and carbon dioxid, and the rest of the 100 per cent. for the total is considered to be nitrogen (including argon). It is customary for a technician to analyze outdoor air once a week, thus to test the accuracy of the apparatus, the efficiency of the absorbing solutions, and his skill in making the tests. The limit of error is given by Haldane as 0.01 per cent., so that successive analyses of the same sample should not differ by more than 0.02 per cent. In routine testing 0.03 to 0.04 per cent. is a common variation to allow for duplicate tests.

The Haldane Apparatus requires:

120 cm. of rubber tubing with heavy walls, inside diameter 3 mm.

120 cm. of special rubber tubing that is "sulfid-free" and will withstand chemical action.

300 c. c. of distilled water.

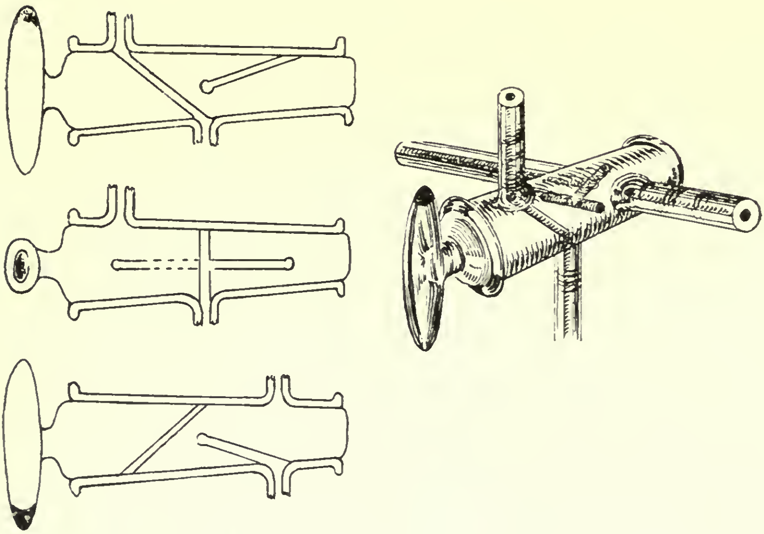
600 grams of stick potassium hydroxid (not purified by alcohol).

10 grams of Merck's pyrogallic acid.

Henderson Gas Analysis Apparatus[2].— The particular features of this type of apparatus are: (1) a 4-way glass stop-cock shown by cut; (2) the adjustment of the volume of the control tube by means of a screw pinch-cock on a bit of rubber tubing on the lower end of the tube; (3) two large test tubes in which the absorbents of potassium hydroxid or sodium hydroxid and potassium pyrogallate are placed.

Buret graduations that are made by average glass blowers are far too rough and inaccurate for the Haldane or Henderson forms of gas analysis apparatus. Thus in some burets, Dr. Henderson states that he has "found the errors of graduation 10 or even 20 times as great as are allowable." He goes on

[2] Applications of Gas Analysis, by Yandell Henderson. The Journal of Biological Chemistry, January, 1918.



SPECIAL 4-WAY STOP COCK

to say: "The absolute error of the instrument was only 0.1 c. c. and this is not greater than is quite common and is allowable for common purposes in an ordinary titration buret. For the calibration of the gas buret the glass blower must not use water but mercury. The standard buret against which he calibrates must be of at least as fine bore as that of the tube of the buret to be calibrated. The standard buret must have been calibrated with weighed amounts of mercury and no mark on the buret purchased should have an error greater than 0.005 c. c."

"The purchaser of a buret should test it before assembling by inverting the buret, connecting it with a reservoir of mercury, filling to the 7, 8, 9 and 10 c. c. marks, respectively, pouring this mercury into a small tarred beaker, and weighing. One c. c. of mercury at room temperature (18°C.) weighs 13.55 gm. An allowance of 0.004 c. c. may be made for the reversal of the

convexity of the meniscus in the inverted buret."

"The correctness of the graduation of the tube of the buret is most easily checked by drawing in on top of the mercury about 0.5 c. c. of water. By raising and lowering the mercury and reading the air-water and water-mercury menisci at various levels (allowing time for the water to drain from the sides) errors of graduation due to irregularities in the caliber of the tube are revealed. The difference in the volume between the two menisci should not vary more than 0.005 c. c. at any two levels."

Chemicals for Henderson Apparatus.—After the apparatus has been assembled and the buret calibrated chemicals are added. The apparatus requires:

350 grams of mercury.

100 c. c. of 10% sodium hydroxid.

100 c. c. pyrogallic solution, made up from 66 c. c. of 30% potassium hydroxid and 34 c. c. saturated aqueous pyrogallic solution.

The potassium hydroxid and the pyrogallic solution should be mixt out of contact with the air, and should make only a yellow or light brown solution, about the color of tea. If exposed to the air during the mixing, the solution becomes darker than this and largely loses its oxygen-absorbing power. In the apparatus both of the absorbents, sodium hydroxid and pyrogallic acid solution, are covered with layers of a few c. c. of liquid petrolatum.

Assembling the Apparatus.— In most respects the apparatus, the technic, and precautions for its use are the same as with the usual form of instrument. Dr. Henderson, however, calls attention to certain features which are liable to be overlooked:

"Red rubber should not be used on the connections where alkali may touch it, as it gives off sulfur which may finally appear as hydrogen sulfid in the buret."

"To make the rubber connections tight (in case of leakage) it is convenient to wrap them with elastic bands. Loop the band around the rubber tube, pull tight, and wrap the free end around the tube several times. Pass a small curved forceps under the wrapping, catch the end of the rubber band over the points of the forceps, and twist the end under the wrapping by withdrawing the forceps. This is a much better method of making joints tight than wrapping them with wire."

"The walls of the buret should always be moistened with a fraction of a drop of 1 per cent. sulfuric acid, and 2 or 3 c. c. of this fluid should be placed in the control tube."

"The analyst must remember that accuracy in the use of the instrument does not depend upon an extreme effort to read the buret as finely as possible, but rather upon making sure that the absorptions are complete. It is therefore common practice, after an analysis is supposedly complete, to pass the gas over again into the absorbent and make another reading to be sure that no change occurs."

"A check on calibration, tightness of joints, and efficiency of absorbents which should be used daily is to make an analysis of atmospheric air. If the apparatus is properly graduated and in good order the sum of the oxygen and carbon dioxid in uncontaminated atmospheric air should be found 20.96 per cent., with an allowable error of ± 0.03 per cent."

Use of Apparatus.— Dr. Henderson in a letter to the Editor, outlines the procedure as follows:

"An unmeasured sample of air is drawn into the buret and past into the pyrogallic until no further absorption occurs. Pass into sodium hydroxid and again into pyrogallic. This leaves the tubes of the apparatus filled only with nitrogen. Proceed with analysis thus:

1. Draw pyrogallic solution and sodium hydroxid to lines marked on stems of absorbers by turning cock to the respective sides and raising or lowering mercury.

2. Turn cock and open buret to outside. Draw small drop of 2% sulfuric acid into buret to moisten the walls. Run mercury to top of stem above cock and connect with sample to be analyzed. Draw sample into buret and bring mercury almost to the 10 c. c. mark.

3. Turn cock to connect with sodium hydroxid absorber and move mercury reservoir until sodium hydroxid rests on line on stem of absorber.

4. Adjust air bulb control until sodium hydroxid in the stem lies on that line.

5. Read gas volume in buret accurately.

6. Pass gas back and forth into NaOH solution by raising and lowering mercury reservoir 5 or 6 times.

7. Bring NaOH to approximately correct level in absorber stem. Bring NaOH in temperature control tube to line by moving NaOH absorber up or down.

8. Bring NaOH in absorber stem accurately to line on stem and take reading No. 2.

9. Turn cock to connect gas buret with pyrogallic absorber and pass gas back and forth slowly 10 or 15 times.

10. Turn cock and pass once into NaOH to take out oxygen in capillary tube. Pass 5 times more into pyrogallic and then draw gas into buret with pyrogallic to proper line on absorber stem.

11. Turn cock to NaOH absorber and take reading as described in (7) and (8).

12. Pass gas into pyrogallic 5 times more and take reading. Continue until no more decrease in volume occurs. Make final reading No. 3. (Repetition of the passage of gas into pyrogallic and repetition of reading No. 3 to constant volume is the chief element in accurate work).

13. Calculate CO_2 percentage of dry gas: Reading No. 1 minus Reading No. 2, divided by Reading No. 1.

Calculate O_2 percentage of dry gas: Reading No. 2 minus Reading No. 3, divided by Reading No. 1.

The use of this apparatus requires some skill and experience in gas analysis. The beginner should be strongly advised to use at first merely the common Orsat gas analysis apparatus. Altho distinctly less accurate than the Haldane apparatus in its original form, or than my apparatus, the Orsat is capable, nevertheless, of giving sufficiently good results for ordinary clinical work and the beginner will not make nearly so many errors."

Calculation of the results of gas analysis and the intermediate steps for computing the metabolic rate are given in Chapter 27, Tables with Explanations.

Qualifications of Analyst.— The person who makes the chemical analyses that are required in the Open Circuit Method, whether the apparatus is of the Gasometer type or the Douglas Bag, must be familiar with this particular phase of gas analysis. A special training is required. In explaining the method that is used at the Mayo Clinic, Boothby states in the Boston Medical and Surgical Journal of September 22, 1921, that "We have not found it difficult to teach high school graduates, in from 4 to 8 weeks, to use a Haldane apparatus accurately." And he further points out that "The principle of a Haldane is very simple, altho it takes some time to acquire the manual dexterity necessary to use it properly."

Benedict says, in the Boston Medical and Surgical Journal, May 16, 1918: "Although the cumbersome gas-analysis apparatus of Zuntz-Geppert has been superseded by the more portable form of Haldane, gas analysis in all its intricacies still remains the bugbear of workers in gaseous metabolism. Furthermore, the gas analyst, to retain his skill, must analyze practically every day."

It is commonly recommended that a technician should have at least a high school education; that to learn the gas analysis method, one month should be spent in some laboratory where daily tests are being made and where routine experience and competent instruction in details may be obtained.

Summary of Apparatus required:

A gasometer of some form, or bag and precise gas meter.
Pipe or tube to outside air.
Rubber tubing.
Face mask, or mouthpiece and nose clip.
Valves, inspiratory and expiratory.
Sampling tubes.
Gas analysis apparatus for determination of carbon dioxid and oxygen contents.
Test tubes and beakers.
Chemical balance weighing to hundredths of a gram and up to at least 100 grams.

Electrically driven shaft to raise and lower mercury reservoir (instead of raising and lowering repeatedly by hand) when several sets of tests are regularly required.

Ground glass with electric lamp in back of it for illuminating the meniscus of the mercury in the buret.

Magnifying glass to aid in taking accurate readings.

CHAPTER 5

GAS ANALYSIS METHOD OF NEW YORK POST-GRADUATE HOSPITAL[1]

By Cameron V. Bailey, M. D.

In equipping the respiration laboratory of the New York Post-Graduate Hospital, we were greatly influenced by the broad experience of Boothby and Sandiford in the clinical application of basal metabolism. Their arguments in favor of the open circuit or gasometer method for institutional work seem to be sound, and, despite the bugbear of gas-analysis, the method is eminently satisfactory.

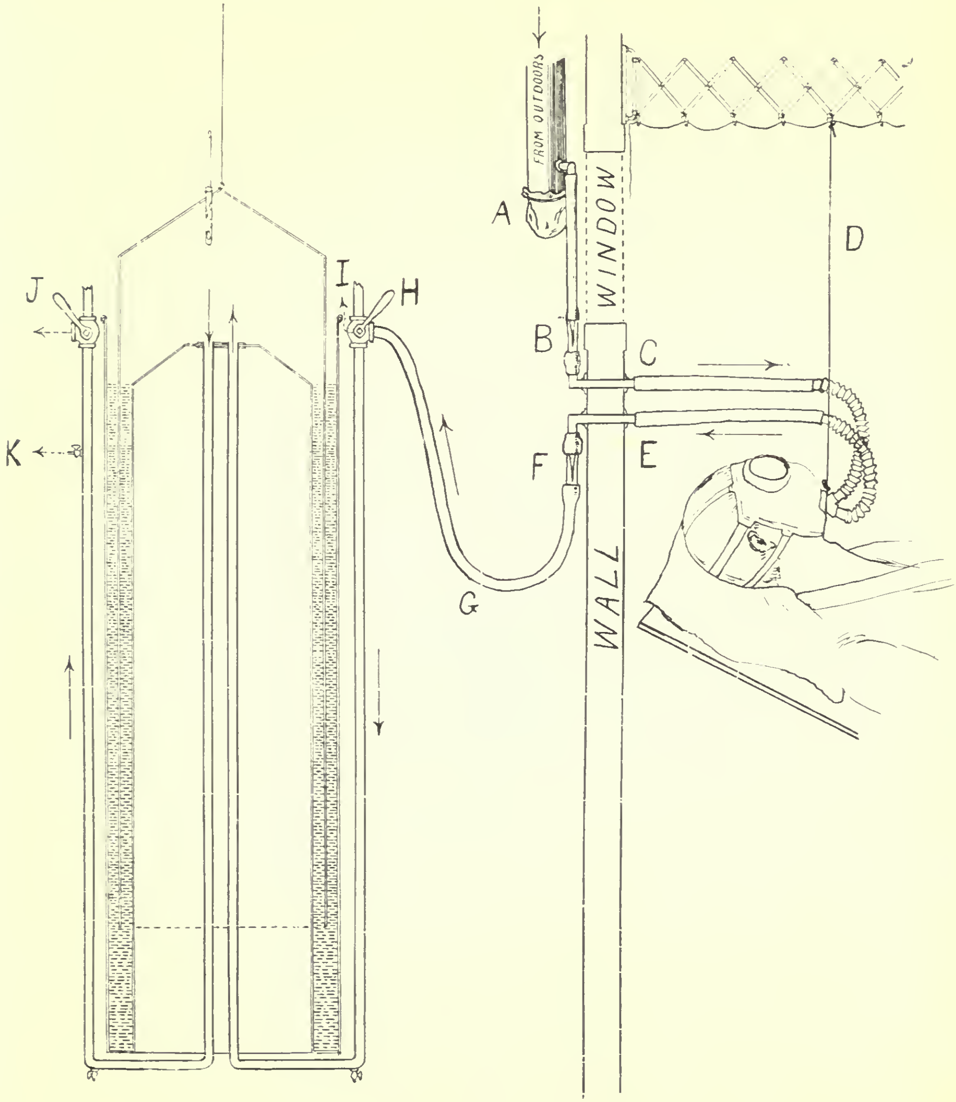
In this method the subject inspires atmospheric air and expires into a gasometer thru a series of tubes, mask and valves. The expired air, having been measured and its volume corrected, is analyzed for carbon dioxid and oxygen; the amount of oxygen absorbed is calculated on a basis of the ratio of expired nitrogen to atmospheric nitrogen. Dividing the volume of carbon dioxid produced by the oxygen absorbed gives the respiratory quotient, which has a known heat value for each liter of oxygen. In this manner the total calories produced per hour may be calculated. Accepting the heat production as practically proportionate to the surface area determined by the Du Bois and Du Bois formula, the calories produced may be exprest in terms of calories per square meter of body surface per hour. This result, the basal metabolism, is usually reported as the percentage above or below the average of the Du Bois normal standard.

By the use of Boothby and Sandiford's calculation sheets, each step in the procedure can be checked by a second assistant, thereby greatly decreasing the chances of technical error. Logarithms, whose name alone has probably inspired dread in the minds of the uninitiated, is an invaluable means of accurately carrying out routine calculations. Employing a Haldane, or one of its modifications, the determination of the carbon dioxid is rapidly carried out before the oxygen analysis.

[1] Editor's abstract of "Apparatus Used in the Estimation of Basal Metabolism," by C. V. Bailey M.D., in the Journal of Lab. and Clinical Med., **6**:657-679, Sept. 1921.

In the Gas Analysis Method (as used at the New York Post-Graduate Hospital,—Ed.) the expired air is collected under most favorable conditions. The subject reclines, the face mask is adjusted, and the test started after the gasometer has been completely washed out with expired air. The test is started and stopt during inspiration without the patient's knowledge, and without his undesirable cooperation. No especial skill is required in this part of the procedure, and, once the apparatus has been tested, the danger from leaks is negligible.

Description of Mask.— The large number of breathing appliances which have been introduced for use with respiration apparatus, is an evidence of the difficulty experienced in finding something suitable for this work. Some device is needed which can be rapidly fitted to any patient, which will permit of his normal type of respiration, which will accurately conduct the inspiratory and expiratory air without offering resistance, and which can be worn in comfort and without danger of leaks. The gas mask of the French army shown in cut below fulfills all of these requirements, when used with the rubber flutter valves introduced by the British during the late war. The mask is made of thick rubber, covers the whole face, and presents broad surfaces which closely engage the forehead, sides of the face and jaw. The tissues in these regions are well supported by the bony framework of the face and the mask readily adapts itself to these fixed surfaces. It is held in place by elastic straps passing around the head. With emaciated subjects, leaks may occur above or below the zygoma; in this area the pull of the straps is in the same plane as the surface of the face. In such instances the leaks are readily overcome by placing 5-inch rubber sponges over these areas of the mask and binding them in place with a 3-inch bandage. In this mask the incoming air is directed upward towards the windows, the opening of the expiratory tube being opposite the nose and mouth; this insures complete ventilation of the space and no discomfort results. When applied to some individuals, the chin pad permits the mask to press on the throat; this can be readily overcome by drawing the mask away from the chin by means of a cord fastened to the tube connections on the mask, and tying the cord to a hook directly over the subject's head. With this cord the mask can be comfortably adjusted, and it has the added value of preventing movement on the part of the patient. Following the test, the mask and attacht tubes are removed from the pipes and are readily cleansed with soap and water.



Pipes, Valves and Connections

Procedure in Making Test.— The first consideration is the handling of the patient; this must be done expeditiously, and in such a way as to allay his fears and to permit of complete bodily rest for a period of at least half an hour before the test is started. During this period the respirations and pulse rate are closely observed and the mask is not applied until the patient appears to be mentally and physically at rest. At this time one also ascertains that the body temperature is normal.

While the subject is resting one empties the gasometer by removing the lower portion of the counterweight and turning the valve (J) — see preceeding cut— to communicate with the room air; the bell sinks until it rests on the obturator and the pointer will stand at zero on the measuring tape. The valve (H) is now turned so as to connect the air-tube (G) with the gasometer. The rubber cap (A) is removed for a few minutes, permitting the large intake pipe to fill with fresh air from out doors; the cap is then replaced.

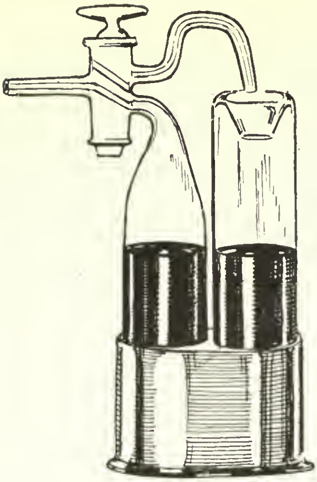
When the patient is sufficiently rested, the ends of the tubes attacht to the mask are dipt in water and slipt over the brass pipes perforating the wall at (*C*) and (*E*), care being taken that the inspiratory pipe leads to the upper openings in the mask. The mask is then applied by holding the chin portion in position and pulling the straps over the top of the head. When accurately fitted, the mask-cord (*D*) is tied to the overhead hook, holding the mask and head in the most comfortable position for the patient. From the time the mask is applied, the inspiratory air is drawn from outdoors thru the pipes to the flutter valve (*B*) and thence to the mask. The expiratory air passes from the mask thru the flutter valve (*F*) and along the tubing to the small space between the top of the bell and the obturator; from there it passes thru the outlet pipe and escapes into the room thru the valve (*J*). In this way the entire dead space of the apparatus is flushed out with expired air.

As an extra precaution, the lower portion of the counterweight is replaced, at the same time closing the valve (*J*). The expirations are now caught in the gasometer. When the bell has been elevated 6 or 8 cm., the valve (*H*) is turned during inspiration, cutting off the gasometer and permitting the expirations to escape thru the vent (*I*). The bell is now dropt nearly to the zero mark by removing the lower counterweight and opening the valve (J). This valve is then closed, the counterweight replaced, and the reading on the tape recorded to the nearest half-millimeter. One is now ready to start the test. The respiratory phases can be readily followed by observing the flutter valves (B) and (F). During the inspiratory phase, the valve (H) is quickly turned to communicate with the gasometer and at the same time one presses the stop watch and the collection is begun. The attendant should watch the subject closely during these procedures and report any movements. While the air is being collected, the respiration and pulse rates are recorded at frequent intervals, and the patient is admonished to remain very still and encouraged by explanations that the test is nearing completion and that everything is very satisfactory. The duration of the test is determined by the subject's rate of ventilation. As a rule the gasometer is nearly filled at the end of 10 to 12 minutes, altho this period may vary from 5 to 15 minutes. Calculation is facilitated by stopping on the minute, the quarter, or the half minute. This is accomplished by holding the stop watch near the inspiratory valve (B) in such a way that both can be observed at the same time; the other hand grasps the valve lever (H); at the selected period of time, and during inspiration, the valve (H) is quickly turned cutting the patient off from the gasometer. Should the subject be expiring, one waits until expiration is completed before closing the valve. The watch is stopt at this time. One must avoid shifting this valve during expiration as it is very disconcerting to the patient. The reading on the steel tape is now recorded to the nearest half-millimeter. The difference between this and the first reading tells the height in centimeters to which the bell has risen. As the bell is exactly counterbalanced in all positions, the inclosed air is under the prevailing atmospheric pressure. The lower portion of the counterweight is now removed leaving the air under positive pressure.

Since volumes of gas vary directly with the temperature and inversely with the barometric pressure, it is necessary to record these factors which will be used later in the calculations. The temperature is determined by a Centigrade thermometer inserted in the bell. A brass-scale mercurial barometer is used in recording the atmospheric pressure.

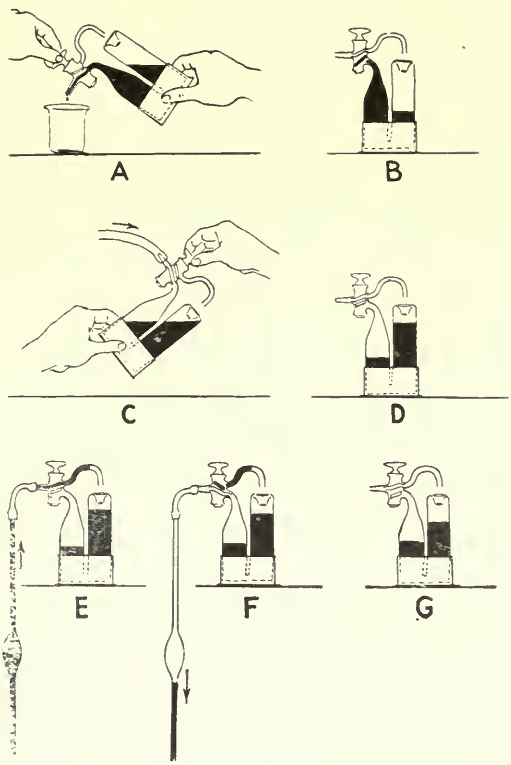
Samples of the expired air can now be collected in gas sampling bottles.

Gas-Sampling Bottles.— The gas-sampling bottle consists of parallel glass cylinders communicating at the bottom thru a small opening. The cylinders are firmly cemented into a metal case which forms a base. The top of one of the cylinders has a funnel-shaped inversion; the other tapers off to a 2 mm. capillary tube to which a 3-way stop-cock is fused. The second opening in the stop-cock communicates with a capillary tube which bends over the inverted top of the first cylinder. The stop-cock terminates in a straight spout of capillary tubing 3 cm. long. The appliance is half filled with mercury, and before use is flushed out with 1 per cent. sulfuric acid. A 6 cm. length of $\frac{3}{16}$ inch rubber tubing is permanently attacht to the spout.



In preparation for use, one sets the stop-cock so that the spout communicates with the gas chamber. The bottle is now tilted forward over a small beaker containing 1 per cent. sulfuric acid, into which the rubber tube dips. The contained air is forced out by the mercury and when the bottle is tilted backward, acidulated water is drawn into the chamber. This position is maintained until mercury drops into the beaker (See *A* in cut). The stop-cock is immediately reversed; this leaves the gas chamber and the lower lead of the stop-cock filled with mercury (*B*), and the spout is in communication with the bent capillary tubing thru which the air to be sampled is blown. Enough acidulated water remains in the chamber to saturate the air when the bottle is filled.

Collection of Air Samples from the Gasometer.— Having removed the lower portion of the counterweight following the final reading of the gasometer, the inclosed air is under positive pressure. The prepared sampling bottle is now placed on the shelf and connected with the sampling-cock. This cock is now



PROCEDURE OF COLLECTING AIR SAMPLES

opened and the air blows thru the curved tube of the sampling bottle. Half the air in the gasometer is allowed to escape thru the outlet valve; this is to insure a fair sample, as recommended by Boothby. The stop-cock of the sampling bottle is now reversed, the bottle removed from its shelf, and tilted backward (*C*) and the compartment fills with the air from the gasometer. The stop-cock is returned to its original position and the sample is trapt under pressure in the bottle (*D*). Before trapping the sample, it is sometimes advisable to tilt the bottle backward and forward several times, at the same time allowing air to escape thru the outlet valve of the gasometer; in this way one is certain of securing a good sample of the inclosed air. Two or three bottles can be filled in this manner, each bottle holding enough air for six analyses.

Principles of Gas Analysis.— The Haldane method is used in determining the amount of carbon dioxid and oxygen in the expired air. In principle, a volume of air is drawn into a graduated buret, where it is saturated with water vapor and measured; the air is then passed back and forth into a potash pipet, where the carbon dioxid is removed; it is returned to the buret and again measured, the difference between this and the first reading representing the volume of carbon dioxid. The oxygen is removed in a similar manner by passing the air into a second pipet containing a potassium pyrogallate solution; after the oxygen is absorbed, the gas is returned to the buret and measured, this second loss in volume representing the oxygen in the sample of air.

These analyses are made in duplicate or triplicate in order to obtain a check for accuracy.

Details of Gas Analysis.— The details of gas analysis are fully covered by the treatises of: Haldane, J. S.; "Methods of Air Analysis", C. Griffin & Co., Ltd., London, 147 pp., $2.00, 1912; and Boothby and Sandiford, "Basal Metabolic Rate Determinations", W. B. Saunders Co., Philadelphia and London, 117 pp., $5.00, 1920.

CHAPTER 6.

KING METHOD: DETERMINATION OF CARBON DIOXID ELIMINATION[1].

By J. T. King, Jr., M. D.

On account of the theoretical variable calorific value of a liter of carbon dioxid, so far it has not been suggested to make use of a simple measurement of the carbon dioxid elimination as an index to the basal metabolic rate. In order to determine this point, it seemed the best procedure to study the original chamber calorimetric work. By so doing we were able to compare the oxygen consumption with carbon dioxid elimination, and also to compare each of these factors with the heat production as measured directly.

Analysis of Direct and Indirect Calorimetry Results. — For this purpose 27 experiments have been analyzed, 10 being taken from the publication of Benedict and Carpenter, and 17 from work by Sonderstrom, Meyer and Du Bois. Each experiment represents an hour's observation, tho in some cases repeated tests were made upon the same subject.

The ten protocols of Benedict and Carpenter were analyzed by the writer as follows:

A. The average carbon dioxid elimination per square meter per hour.

B. The average oxygen consumption.

C. The average heat production.

On the basis of these averages the deviation of carbon dioxid from its average was calculated for each experiment. The deviations of oxygen consumption and heat production from their respective averages were also calculated for each experiment.

[1] Editor's abstract, "Determination of the Basal Metabolism from the Carbon Dioxid Elimination, with a Statistical Note by Raymond Pearl", The Bulletin of the John Hopkins Hospital, Sept., 1921. Approved by author.

The carbon dioxid deviation from its average was then compared directly with the deviation of heat production from its average in each experiment. A similar comparison was made between oxygen consumption and heat production. It was found that the

Average difference between carbon dioxid variations and calorie variations was 4.93%
Average difference between oxygen variations and calorie variations was 8.39%

An analysis was made in a corresponding manner of the data of Sonderstrom, Meyer and Du Bois. In this series the calories calculated by the indirect method are also published. It must be remembered that the technic of these early observations with the chamber calorimeter included not only the oxygen consumption and the carbon dioxid elimination but urinary nitrogen determination as well. By these means, the nitrogenous metabolism was estimated, and the oxygen and carbon dioxid figures were partitioned and calculated for protein and non-protein oxidation. The indirect method used in connection with the chamber calorimeter may, therefore, be taken as ideal. This analysis showed that the

Average difference between the indirect and direct calorimetric figures was 3.79%
Average difference between the carbon dioxid and direct calorimetric figures was 4.73%
Average difference between oxygen and direct calorimetric figures was 5.70%

A third series of protocols (Benedict, Emmes, Roth and Smith) was studied chiefly for the purpose of obtaining a scale of standard figures for the carbon dioxid elimination in a large number of normal individuals. In this series we have not attempted to draw conclusions as to the correlation of the oxygen and carbon dioxid figures, respectively, with the calories, inasmuch as the calories are calculated calories (indirect method), and not measured calories (direct method). The calorie figures follow the oxygen figures more closely than they follow the carbon dioxid figures. It is, therefore, obvious that the practical result of the customary method of deriving calories from oxygen and carbon dioxid figures is that the oxygen figure is more influential in determining the resultant calorie figures than the carbon dioxid figures.

In the results of these analyses let letters have the following significance:

A. Carbon Dioxid per square meter per hour in grams.

B. Oxygen per square meter per hour in grams.

C. Calories per square meter per hour.

r. Coefficient of correlation between the two variables indicated by attacht letters.

PE. Probable error.

The significant comparisons are:

Direct calorimetry (10 cases)

$r_{AC} - r_{BC} = .719 - .488 = +.231 \pm .192$ Diff P.E.$_{DIFF} = 1.2$

Direct calorimetry (17 cases)

$r_{AC} - r_{BC} = .846 - .836 = -.010 \pm .068$ Diff P.E.$_{DIFF} = 0.1$

From these results it must be concluded that the oxygen intake is not significantly more highly correlated with directly measured calorie output than is carbon dioxid. The differences in the correlations are sensibly zero, having regard for these probable errors. In the longer series (17 cases) the correlation is actually slightly (but not significantly) higher for the carbon dioxid with calories than for the oxygen with calories.

Proposed Scale of Normal Figures.— In order to test the method which has just been described, a series of 17 observations was made upon normal subjects. Each observation included a preliminary period and 15 minutes of carbon dioxid collection. The results show that an average of 12.83 grams carbon dioxid per square meter of body surface per hour is eliminated by healthy men whose ages lie between 20 and 40 years.

On the basis of this standard figure, a prediction was made by the writer of carbon dioxid elimination for various ages and for both sexes. These results are based upon the curve constructed by Aub and Du Bois, showing the heat production of healthy males at various ages. These predicted values were then compared with the actual values observed by Benedict and his associates — obtained by the analysis of Benedict's figures by decades. The correlation between the two sets of figures was close for the decades in which actual observations were made: those of Benedict and others are 13.13 grams and 12.89 grams per square meter per hour for the third and fourth decades respectively. The author's figure for the third and fourth decades together is 12.83 grams. A satisfactory scale of normal figures may therefore be obtained by taking an average between Benedict's and the author's figures for the lower decades. For decades above the fourth it seems to the writer safer to allow the carbon dioxid figures predicated upon the curve of Aub and Du Bois. Such a proposed scale is as follows:

GRAMS CARBON DIOXID ELIMINATED PER SQUARE METER PER HOUR

Proposed Scale of Normal Figures

Age	*Men*	*Women*
15-20	14.03	12.75
20-30	12.98	11.95
30-40	12.86	11.85
40-50	12.52	11.74
50-60	12.21	11.37
60-70	11.86	11.05
70-80	11.53	10.71

Description of the Apparatus.—The apparatus for collecting and measuring carbon dioxid elimination is quite simple. The method is open, the older U. S. Army gas-mask being used to deliver outside air to the subject and to carry expired air to the tubing leading to the 3 jars. The gas-mask canister, seen hanging from the horizontal bar, is emptied by removing the valve in the bottom, removing the contents and sealing the valve into place again. On the intake side, then, there is nothing between the patient and the outside air except a light rubber valve in the bottom of the canister, which rises and falls with respiration.

Expired air passes thru the flutter-valve out of the gas-mask and is caught in a rubber cuff, that is sealed with paraffin about this outlet valve. The cuff tapers into rubber tubing and the expired air passes thru the 3 collecting jars.

Resistance to the passage of air thru the jars has been measured by inserting a water manometer between the subject and the first jar. Observations upon 2 large men showed an average momentary rise of pressure of 6 to 8 millimeters of water. On

Apparatus and Balance for Measuring Carbon Dioxid Elimination deep respiration the pressure rose occasionally with a quick elevation, such as one sees in a water hammer pulse, to 14 millimeters of water. Such pressure changes, it was thought, made a fan superfluous. There is no inspiratory effort whatever.

The 3 jars are identical in construction and are such as were part of the original portable apparatus. Incoming air is carried thru a tube almost to the bottom of the jar. Here it is scattered thru a cone with multiple perforations, filters upward thru the chemicals, and passes out at the top.

The first jar contains 4-mesh calcium chlorid. This has been found to desiccate expired air completely.

The second jar contains soda lime and absorbs the carbon dioxid from the dried air. To insure the efficacy of soda lime it should be changed after it has taken up a total of 75 grams of carbon dioxid.

The third jar contains calcium chlorid of the same type as that used in the first jar. This third jar is necessary because the soda lime (jar 2) contains a rather high percentage of moisture, some of which is carried out of jar 2 during each test; jar 3 absorbs this vapor. The increase in weight in jar 3, therefore, must be added to the net increase in weight of jar 2 in order that the determination of carbon dioxid may be correct.

Test for Leaks.— The test for leaks should be made frequently. While someone is breathing into the apparatus, go over the joints of the apparatus with a soft brush with soap suds. Formation of a bubble will indicate a leak.

Ventilation Test.— The ventilation is practically always free with this method, the only difficulty being possible occasional adhesions of the moist valve. It is an advantage to have the flutter valve encased in some sort of glass chamber which can be opened, thus affording a means of drying the valve.

Technic of the Test.— The patient is prepared in the usual way, as described on page 45. The room is well ventilated before and during the examination, the patient being carefully protected from the cold. After the mouthpiece and nose clip are adjusted, the patient is instructed to be quiet and to breathe naturally. For several minutes a preliminary period is carried out, the patient breathing thru the first jar only. This is done in order to allow the patient to become used to the procedure, and the length of this preliminary period depends upon the readiness with which he settles down to his task. It is found that most complaints arise during the very beginning of the test. If a new start must be made, it is, therefore, usually accomplished during this preliminary period, and it is not necessary to re-weigh jars 2 and 3. As soon as the patient is quiet and breathing smoothly, jars 2 and 3, which have been previously attacht to each other, are joined to jar 1, note being taken of the time to the second. The expired air is past thru all these jars for 10 minute periods, these 10 minute periods being repeated until 2 of the results agree reasonably closely.

Calculating the Metabolic Rate.— The metabolic rate is calculated as follows: The sum of the increase in weight in jars 2 and 3 represents the carbon dioxid elimination. The carbon dioxid for 2 periods is added and multiplied by 3. This gives the carbon dioxid elimination per hour. This is divided by the body surface, (Du Bois height-weight chart). The resultant figure — grams carbon dioxid per square meter per hour — is our end result. This is compared with the standard normal figures and the percentage deviation from the average normal figure is calculated.

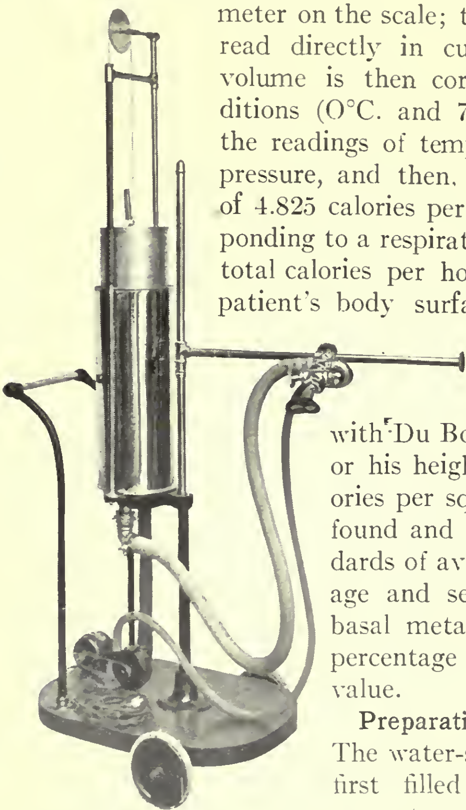
CHAPTER 7.

SANBORN BENEDICT APPARATUS

By Henry Elsner Marks, M. D.

Indirect Calorimetry.— With the Benedict Portable apparatus the metabolic rate is calculated from measurements of oxygen consumption over a given period of time. This is the method of indirect calorimetry from one of the respiratory gases, and it is based upon the assumption that each liter of oxygen used liberates a definite amount of energy from the food substances in the body; in other words, that the respiratory quotient is constant. Observation has shown that this assumption is justified when the subject is in the fasting state. Except in conditions in which the metabolism of certain of the foodstuffs is interfered with, as in diabetes mellitus, the proportions of stored protein, fat, and carbohydrate metabolized by the fasting subject are quite constant. This fact permits us to assign a definite heat value to a given quantity of either oxygen or carbon dioxid, and, since Murlin and Lusk and others have shown that the values obtained by indirect calorimetry agree closely with those obtained by the direct measurement of heat elimination in the calorimeter chamber, we are justified in considering as accurate the calculated values obtained by this method.

Description of Apparatus.— The apparatus gives accurate determinations of oxygen consumption by measuring the change in volume of the gas in a closed circuit, the carbon dioxid produced being absorbed by circulating the air through soda lime. A gasometer with an accurately balanced bell is included in the circuit; the rest of the circuit, with the exception of the lungs of the patient, is of fixed volume, so that a change in height of the gasometer bell indicates a change in total gas volume, provided the lungs are at the same phase of respiration when all measurements are made. The counter-weight of the gasometer bell bears an index and the height of the bell is read on a scale at the beginning and end of a measured period; from the readings of time and total change in volume the oxygen consumption per minute is calculated. With the older machines the scale read in millimeters, and volume was found by multiplying the number of millimeters shrinkage by a factor representing the volume corresponding to one millimeter on the scale; the more recent machines read directly in cubic centimeters. This volume is then corrected to standard conditions (0°C. and 760 mm. pressure) from the readings of temperature and barometric pressure, and then, using an assumed value of 4.825 calories per liter of oxygen (corresponding to a respiratory quotient of .82) the total calories per hour are calculated. The patient's body surface having been determined from the height and weight measurements, in accordance with Du Bois' height-weight formula or his height-weight chart, the calories per square meter per hour are found and compared with the standards of average values, based upon age and sex. This then gives the basal metabolic rate in terms of percentage of the average normal value.



Preparation of the Apparatus.—The water-seal of the gasometer is first filled with water at about room temperature, to within 3 or 4 inches of the top of the tank. In order to prevent accidental spilling into the air chamber and circulation tubes when the machine is not in use, it is well to draw off a portion of the water after the completion of a test, and if this is kept in the vessel into which it is drawn it will be at room temperature when the machine is next used and can be poured back into the tank without disturbing the temperature of the gas. The fan motor and fan shaft bearings are now oiled, the motor started, and the test of ventilation rate is made.

The fan should deliver approximately 30 liters of air per minute past the mouthpiece, and its ability to do so should be tested each day that the machine is to be used. The test is best carried out by measuring the time required for the fan to empty the gasometer completely. The afferent tube (the smaller one) is first disconnected from the mouthpiece, the gasometer bell is raised to its highest point and the mouthpiece connection from which the tube was removed is closed with a cork. The motor is now started, the bell released, and its descent timed. It should empty itself in about 15 seconds. If more than 18 seconds are required, the fan or motor needs attention, or the absorber is packed too densely. When the ventilation test is completed, the machine is tested for leakage.

A leakage test should be made each day that the machine is to be used as well as each time any changes are made in the joints or connections of the air circuit. The test may be made with the motor running, or turned off; a 100-gram weight is placed on the gasometer bell and volume and temperature readings are made over a period of several minutes, preferably at least 10 minutes or the length of a metabolism test period. With the temperature constant there should be no change in volume during this time, provided the gas has been well circulated and thoroughly mixed before making the first reading, so as to be of uniform temperature throughout. If the temperature changes during the test there will be a corresponding change in volume: this amounts to about 40 cc. for each degree Centigrade in the older form of apparatus with soda-lime jar outside the gasometer, where the total volume with one jar in the circuit is about 10 liters.

A complete leakage test should also include a test for negative leaks, especially with the form of apparatus in which the absorbing jar is placed before the circulating fan in the circuit, as here a higher degree of negative pressure may develop. The test is carried out in a manner similar to the ordinary test except that a weight is attached to the counterbalance cord of the gasometer instead of being placed upon the bell. This test need only be carried out occasionally, or when the connections between the gasometer and the fan have been changed.

With the gasometer nearly empty, oxygen is now admitted until the bell is well filled. About 4000 c.c., or 20 cm. on the scale, usually suffice for a patient of medium size; with an elevated metabolic rate or a large patient, more should be allowed. The introduction of the compressed gas lowers the temperature and the gas should be circulated for several minutes and mixed thoroughly before making preliminary readings; time may be saved by making the leakage test after admitting the oxygen instead of before.

Making the Metabolism Test.— The test itself consists in making readings of the gas volume on the gasometer scale at the beginning and end of a measured period of time. Since the lung volume must be the same at the time of making each reading it is customary always to read the scale at the end of a normal expiration. Usually, with the patient at rest and comfortable, the lungs empty themselves to almost exactly the same point with each expiration; therefore the change in the scale reading with each successive descent of the index represents the oxygen absorbed during that respiration. Irregular expirations, however, deeper or shallower than the average or normal ones, are always more or less numerous, and if the scale is read at the end of one of these considerable error may be introduced. In order to avoid this, the scale is watched carefully over a series of expirations and from observation of these readings an idea is formed of the regularity of expiration and of the average shrinkage with each respiration. When a series of 3 or 4 expirations occurs which are apparently normal and show regular shrinkage the correct reading of the next expiration can be estimated from them; the time reading is taken at the moment of this next expiration and the estimated correct value is taken as the scale reading regardless of whether or not the index actually stopped at that point. The accuracy of this estimated reading may be further checked by watching one or two expirations immediately following the one taken. Readings both before and after the one taken can be made, of course, only when the patient is breathing into the circuit both before and after the reading; that is, with the so-called "flying start," or with inside readings by the Emmes method. With the outside readings, when the period is started or ended with the turning of the valve, the check readings are made only after or before the one recorded, as the case may be.

The period is started, then, by turning the valve at the end of a normal average expiration, and at the same moment starting the stopwatch. The next 2 or 3 expirations are watched and the correct initial reading estimated from them and recorded on the data sheet, together with the temperature. At the end of the period readings are again made on each of several successive expirations, the reading for the next expiration is estimated from them, and when the index descends to that point, the valve is again turned and the watch stopped. If the operator is not successful in turning the valve at the point which he estimated as correct, the error is noted; after the gas is washed the final reading is corrected by the amount of this error.

After turning the valve the gasometer continues to descend for a minute or two, usually shrinking from 80 to 200 c. c. before coming to rest. This is due to the washing out of carbon dioxid and water vapor, and since the period was started with dry air free from carbon dioxid the final reading is not made until the residual air is again dry and free from carbon dioxid. This reading is then corrected if necessary and recorded on the data sheet together with the final temperature reading.

Readings are estimated to tenths of a millimeter, or to 10 c. c. on the volume scale, for greater accuracy.

Check values are obtained by determining the oxygen consumption over measured portions of the test period by the Emmes method. These are termed "inside readings", and it is customary to take two inside readings after the start of the period and two before the end, giving two inside periods, each from 6 to 8 minutes long. It must be remembered that atmospheric conditions inside the machine during the period are different from those found at the beginning or end, since both water-vapor and carbon dioxid are present to a degree depending upon the rates of their production and absorption. This point of equilibrium between production and absorption is reached only after an appreciable period of time, and since water-vapor and carbon dioxid content should be the same at both beginning and end of the inside periods, it is best to wait a minute or two after the start of the period before making the first inside reading. This reading is estimated in the manner described from the readings of the preceding and succeeding normal expirations, and the time noted at the instant of full expiration, without stopping the watch. Temperature is then noted, and the 3 readings recorded upon the data sheet. The initial reading of the second inside period is then made in the same way, and toward the end of the period the final readings of the inside periods are made. Thus 3 checks are obtained for each period. It is the practice of some operators to dispense with the outside reading and to make all 3 readings by the inside method. I believe, however, that if good checks can be obtained by 2 different methods the results are more reliable, and, therefore, prefer to follow Benedict's original technic, as here outlined.

During the period the patient's pulse and respiration rates are noted, as well as the barometer reading.

At least 2 periods, giving 6 check readings, should be obtained. Oxygen consumption per minute is calculated at once for each of the 6 readings and if the results show a variation of less than 3 per cent., no further readings are necessary. If not, another period should be run. It will then usually be found that the second and third periods give satisfactory checks, the higher value of the first period being due to nervousness, restlessness or irregular breathing at the beginning, and before the patient became accustomed to the procedure.

Method of Calculation.— The first step in the calculation consists in the determination of the average oxygen consumption per minute. On the data sheet have been recorded for each period the figures of total shrinkage, duration of period, and temperature at start and end of the period. If the shrinkage is read in millimeters on the gasometer scale it must be converted into cubic centimeters by multiplying by the factor supplied with the apparatus which indicates the volume of gas corresponding to 1 mm. on the scale; if the scale reads directly in cubic centimeters this step is not required. Next, from the barometric pressure as observed the gas volume is corrected to 760 mm. by multiplying by $\frac{P}{760}$. This volume is then corrected to 0°C. by temperature correction tables, or by multiplying by $\frac{1}{1+.00366t}$ t being the mean temperature during the period. This corrected volume is now divided by the number of minutes duration of the period (fractional parts of a minute being converted from seconds into decimal parts by a table) and the oxygen consumption per minute is found.

A correction must be applied to this figure because of error in the method of making the temperature correction. This should properly be done by correcting the total volume of gas in the circuit at the beginning and at the end of the period to 0°C. and subtracting the two to obtain the total shrinkage. With the method used, however, we do not measure the total volume of gas in the circuit but only the change in volume, and then apply the temperature correction to the amount of shrinkage found. The error imposed by this procedure amounts to about 1.8 c.c. for each degree Centigrade of rise in temperature during the period, added to the oxygen consumption per minute.

As mentioned above, the figures for oxygen consumption should show a maximum range of variation within 3 per cent.; that is, the extreme values should be within 10 c.c. of one another for an oxygen consumption in the neighborhood of 250 c.c. per minute. If a greater variation is present an effort should be made to find the source of the discrepancy. The first 2 periods may show a considerable difference; as has been mentioned, this may be due to initial discomfort in breathing with the mouthpiece and nose-clip, and a third period will give figures agreeing with the second. If the first 2 periods give good checks a third period is unnecessary. There will then be 2 periods, with 6 check values in all. If we have been fortunate enough to have had a patient who breathed regularly, or if, with irregular respiration, we have been able to estimate our scale readings correctly, it will be found that at least 4 of the 6 checks fall within an extreme variation of 4 or 5 c.c.; one or two may fall wide of this group through error in observation or estimation and these are discarded in calculating the average. With less favorable conditions the values may all be more or less widely scattered. If at least four of them fall within the range of 3 per cent. variation they may be considered satisfactory, but with greater variation the relative value of the test must be considered impaired and the weight of the evidence which it is depended upon to contribute is correspondingly lessened. In such cases it is worth while to calculate 3 values of the metabolic rate, one from the average oxygen consumption, and one each from the maximum and minimum values obtained. This procedure gives a clearer idea of what the test is worth in such cases.

Having determined the average oxygen consumption per minute, the energy equivalent of this quantity is found by multiplying by 4.825, the number of calories of energy liberated by 1 liter of oxygen under the conditions of the test; that is, in the post-absorptive state, when the fuel burned gives a respiratory quotient of .82. Multiplying this product by 60 gives the total calories produced per hour. This is now divided by the number of square meters of body surface to find the calories per square meter per hour, and finally, this quantity is divided by the normal average value for an individual of the same sex and age to determine the percentage variation from the normal standard.

All these steps are performed most easily and simply by the use of logarithms. As illustrated in the accompanying figure, total oxygen consumption for each period is found by adding the logarithms for the spirometer factor (the constant supplied with the machine), the shrinkage factor (these two are combined when the scale reads in centimeters), the barometer factor, and the temperature factor. Tables are obtainable which give directly the logarithms for these last two factors. (See page 256). The barometer reading is corrected first for temperature (of the barometer itself); this correction is taken from a table and subtracted from the observed reading. The corrected reading is then used to find on the barometer table the logarithm for the barometer factor. From the mean temperature for the period the logarithm for the temperature factor is similarly found on another table. The sum of these four (or three) gives the logarithm of the total oxygen used; from this is subtracted the logarithm of the duration of the period, and the antilogarithm of the difference is the oxygen per minute in cubic centimeters. To this is added the correction mentioned above of 1.8 c.c. for each degree Centigrade rise in temperature during the period, and the average oxygen per minute is then obtained.

To convert this into calories the logarithm of average oxygen per minute is added to the logarithms of 60 and of 4.825; the antilogarithm of the sum is the number of calories produced per hour. Subtracting the logarithm of the number of square meters body surface gives the logarithm of calories per square meter per hour, and subtracting the logarithm of the standard value from this gives the logarithm of the percentage variation from the standard. In all these operations the characteristic of the logarithm is omitted, only the mantissa being used.

The body surface is found from the measurements of height and weight by Du Bois' height-weight chart, or calculated from these measurements by his height-weight formula, according to which:

$$\text{Log of body surface} = 0.425 \log \text{weight} + 0.725 \log \text{height} + .85634$$

Location of Leakage.—The importance of testing the machine frequently for leakage has already been mentioned. Error from an unsuspected leak is, of course, inexcusable and can only result from carelessness in technic. When the test shows that leakage is present it is often troublesome and difficult to find the source; we have found the following method to be most effective.

The gasometer is first isolated from the rest of the circuit by removing the bell and closing the inlet and outlet tubes with rubber stoppers. If the inlet has wires soldered across it so that a stopper cannot be introduced, the inlet tube connection below the gasometer is unscrewed and the stopper used to close the tube at this point. A Y-tube connected with a blood-pressure bulb and manometer is then connected to the oxygen inlet or to a tube passed through one of the rubber stoppers, and the pressure in the circuit is raised to about 100 mm. of mercury. By listening carefully now at all points of the circuit, the hiss of the escaping air can usually be heard, and the exact location of the leak is then found by painting the suspected area with soapsuds. If nothing can be heard the soapsuds must be used on one part of the circuit after another until the leak is found. The fault is usually found about one of the joints, especially those in which washers are used, and is then easily remedied. The fan is also apt to leak, especially about the gasket, as the pressure is greatest here when the motor is running, and it may also show either a positive or negative leak about the fan-shaft. This should fit well in its bushing and should be kept well oiled.

Activity of Absorber.—The most convenient index of the activity of the soda lime is the magnitude and rate of shrinkage at the end of the period after the patient has been cut off from the machine. With a normal ventilation rate and active soda lime the air in the gasometer should be washed free from carbon dioxid and water-vapor in not much more than 1 minute; the descent of the bell should have stopped in that time, and the total shrinkage during the washing period should not be much above 150 c.c.,—with fresh sodalime it does not go above 80 c.c. The special soda lime now obtainable, of the submarine type, is especially active. The ordinary soda lime is not active if too dry and should be moistened a little when first used; with continued use it may become so wet as to cake and retard the circulation of air, in which case, if the machine has outside absorber jars, a calcium chlorid jar may be introduced in the circuit before the soda lime. The dried air will then take up moisture from the soda lime and so improve its efficiency.

Irregular Respiration.—This is the commonest and most serious cause of error. The validity of the test depends fundamentally upon accurate measurements of gasometer volume and accuracy of these measurements requires that all readings be made at the same point in the respiratory cycle. Consequently it is of the greatest importance that the scale be watched carefully and the reading of each expiration made for at least half a dozen respirations before a reading is taken; in the case of the reading at the start of the period the expirations immediately following the initial reading should be noted carefully. The correct reading is then predicted from the preceding ones, and it may be checked by reading also 1 or 2 expirations following it. This procedure will give satisfactory results with regular breathing or with the usual case in which there is only slight irregularity. With the type of case in which irregularity is extreme it may be impossible to determine or estimate any normal point of expiration, and in such cases a satisfactory determination of oxygen consumption is impossible. Several periods should be tried, however, before the attempt is given up, for not infrequently the respiration becomes more regular as the patient becomes accustomed to the machine.

Variations in the Respiratory Quotient.—The normal patient in the post-absorptive state shows a respiratory quotient close to .82, which corresponds to a heat value of 4.825 calories for each liter of oxygen consumed. In this state the proportion of carbohydrate, fat and protein utilized by the body is quite constant. During digestion and absorption, however, the proportions depend upon the previous food intake, and the heat value of a liter of oxygen may vary between the extremes of 4.686 calories and 5.047 calories, so that the importance of the preliminary fast is manifest, entirely aside from the effect of food in elevating the metabolic rate. In diabetes the normal ratio of utilization of the various foodstuffs is disturbed, and the respiratory quotient changes, so that in this condition determinations of the metabolic rate are not reliable unless they include the determination of carbon dioxid elimination and the calculation of the respiratory quotient. Even then, if there is acidosis, with disturbance in the carbonate reserve of the body, and with incomplete combustion of fat, and the elimination of ketones through the kidneys or lungs, the relationship between the respiratory oxygen and carbon dioxid cannot give accurate information of the food substances undergoing combustion or of the heat liberated by a definite quantity of oxygen. In such cases, therefore, indirect calorimetry is not to be relied upon.

Length of Period.— It should be remembered that each minute added to the period decreases the error due to inaccuracy in making the scale reading. It is best, therefore, to make the periods as long as possible. A duration of more than 15 minutes, however, is likely to make the patient restless, and if the oxygen consumption is high the capacity of the gasometer limits the duration to about this length.

In addition, there are a number of minor sources of error that must be guarded against. Restlessness and nervousness of the patient must be reduced to a minimum, and if present should be noted so that this circumstance may be taken into consideration in judging the result of the test. The pulse rate during the period should always be noted. The increased muscular work when tachycardia, tachypnea, or tremor is present may cause considerable elevation of the rate, so that these conditions should always be noted for the same reason. Error may be introduced by the swallowing of air. In order to estimate correctly the significance of these factors the patient should be watched constantly during the test.

It is not necessary to correct the barometer reading for water vapor tension. If the air were saturated when one reading is made and dry when the other reading is made the error would amount to less than 3 per cent., but as a matter of fact the air is practically dry when the outside readings are taken, and is presumably at about the same percentage of saturation when all inside readings are taken. Under such conditions the difference between the readings represents oxygen consumption alone and water-vapor tension need not be considered.

DATA SHEET

Period	*Scale readings*	*Time*	*Temp.*
I.	Start	End	End
	End	Start	Start
	Shr.	Dur.	Diff.
			Aver.
Ia.	Start	End	End
	End	Start	Start
	Shr.	Dur.	Diff.
			Aver.
Ib.	Start	End	End
	End	Start	Start
	Shr.	Dur.	Diff
			Aver.

Data sheet for a single period, with two inside periods.

CALCULATION SHEET

	I.	*Ia.*	*Ib.*	*II.*	*IIa.*	*IIb.*
Duration (dec.)						
Shrinkage						
Average temperature						
Temp. difference						
Correction						
Logarithms.						
Log spirometer factor						
Log barometer factor						
Log temperature factor						
Log shrinkage						
Log total oxygen						
Log time						
Log oxygen per min.						
Oxygen per min.						
Correction						
Corr. oxygen per min.						
Average oxygen per min.						
Log av. oxygen per min.						
Log 60	68350				Height =	
Log 4.825	77815				Weight =	
Log calories per hour		=	calories per hour		Body surface =	
Log body surface ( )					Age =	
Log cal. per sq. meter.		=	calories per sq. m. per hour		Pulse rate =	
Log normal standard ( )					Resp. =	
Log % variation		=	% normal average basal rate.			
					Barometer	mm. at °C.
					Corr.	
					Corr. bar.	mm.

CHAPTER 8

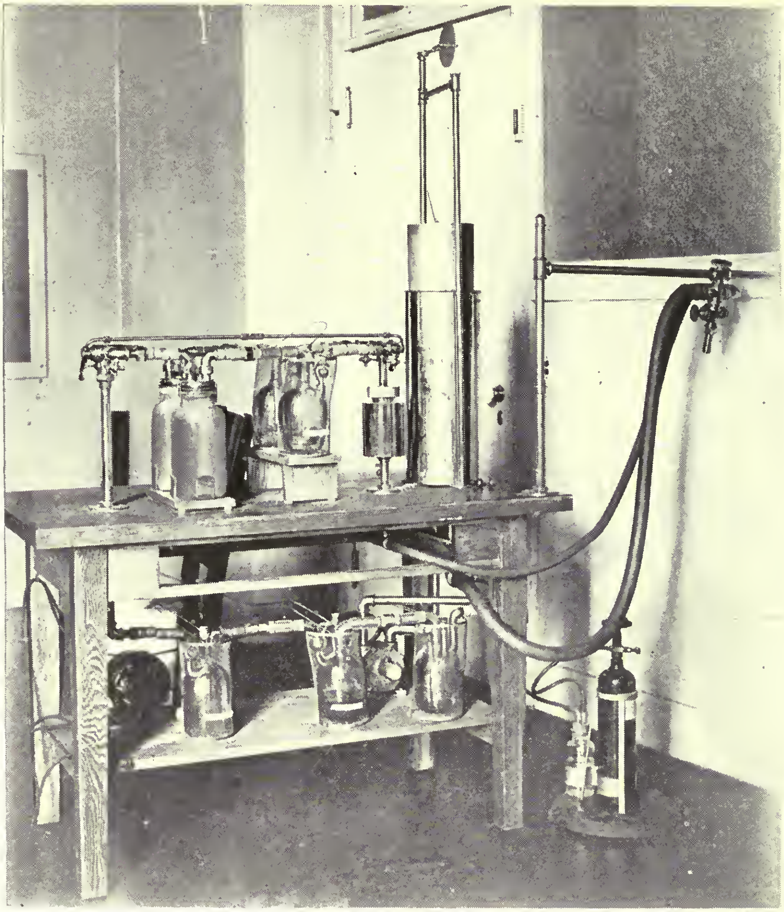
BENEDICT UNIVERSAL APPARATUS

By Lovell Langstroth, M. D.

[The Apparatus and Method here described are in use at the Hospital of the University of California, San Francisco, Cal. It is a part of the service equipment, not for research. With it two to three patients are tested each day. The editor had opportunity at a recent visit there to see the thoroness and scope of the laboratory equipment of which this apparatus forms an integral part. It is modern equipment, well-kept, and systematically used.

The chapter describes: Testing the Apparatus (before a patient is tested); Measuring the Oxygen (that a patient consumes); Measuring the Carbon Dioxid (that a patient exhales); Preparation of Patient; Making the Test; and Calculating the Results. — Editor.]

Testing the Apparatus.— In setting up the apparatus (see illustrations on next page) the operator should first familiarize himself with the different parts and have clearly in mind the path which the current of air takes in going thru them. Beginning at the threeway valve near the mouthpiece the air passes by way of the large rubber tube directly into the spirometer. This allows for expansion and contraction of the volume of the closed circuit and affords at the same time by means of the graduated scale a method of measuring the O_2 (oxygen) consumed. From the spirometer outlet it passes to the blower which affords the positive pressure necessary to force the current thru the various acid and soda lime bottles. The air passes from right to left thru the Williams absorbers on the lower shelf of the apparatus where it is dried. The absorber bottle on the extreme right is kept empty to act as a guard against the entrance of acid into the pump in case of possible reversal of the direction of the current. The glass inlet tube should be turned to the left with the direction of the air current. The next two absorbers contain concentrated sulphuric acid and the inlet tubes should be turned to the right against the direction of the air current. They should not be filled more than one-half inch above the air



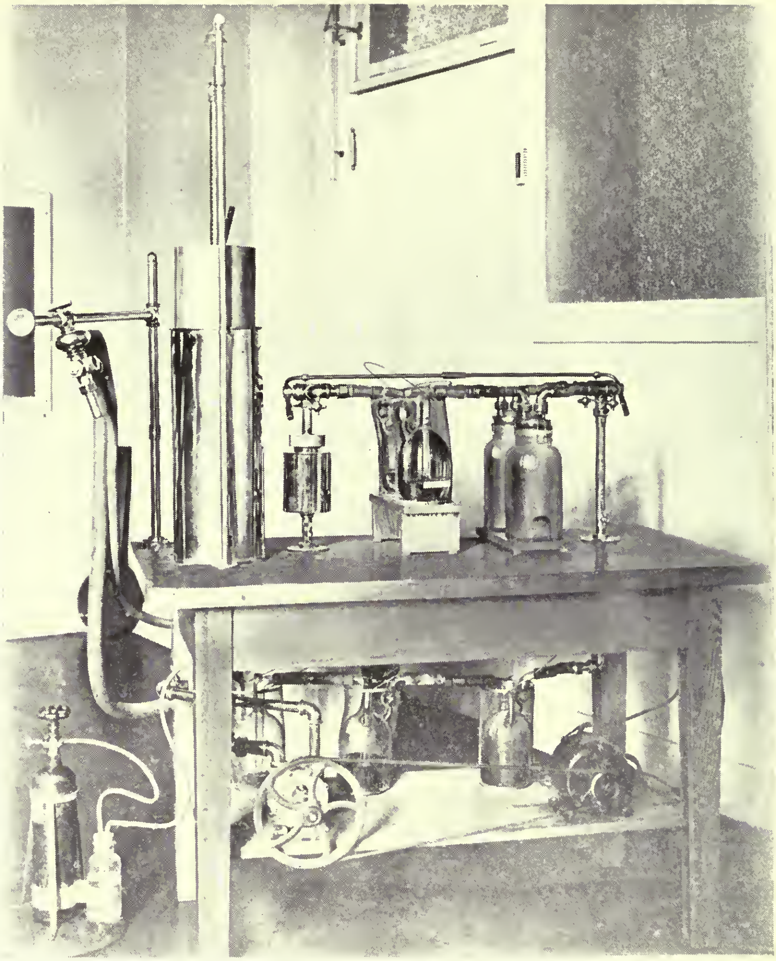
Front View of Universal Respiration Apparatus

The Williams absorbers on the lower shelf contain sulphuric acid. The motor and blower are shown behind them. On the top of the table are the soda lime bottles, the sulphuric acid bottles to catch the moisture from them, the sodium carbonate can, and the spirometer.

holes. We have found it advisable to mark the level to which acid is added in the absorbers by means of a narrow strip of adhesive fastened on the wire basket container. This indicates the amount of water absorbed by the acid. The acid in the first absorber should be changed sufficiently often to keep that in the second at its maximum concentration. The dried air is now led through the soda lime container where the CO_2 (carbon dioxid) is absorbed. Moisture taken up from the soda lime is caught by the concentrated sulphuric acid in the Williams absorber thru which the air then passes and any change in the weight of these two bottles will indicate the mass of CO_2 absorbed from the circulating air. The air inlet of this absorber should point to the left against the air current. Any acid fumes in the air are absorbed in the Sodium Carbonate can. A small piece of fine wire gauze is placed over the outlet tube at the bottom and the can then filled three-quarters full with alternate layers of cotton wool and sodium carbonate. From here the air is led thru the smaller rubber tube back to the three-way valve at the mouthpiece. The dried air can be led thru either of the two soda lime bottles by turning the double valve which connects the CO_2 absorption bottles with the remainder of the apparatus. This is a matter of convenience when large amounts of work are being done with the machine.

The spirometer should be filled with water to within 3 inches of the top and the bell should swing free of the sides. In setting up the two uprights which support the spirometer pulley the cross arm at the top should be adjusted so that they will be parallel when in position. Convergence or divergence of these supports will tend to throw the spirometer bell away from its center. The table itself should be carefully leveled as this, too, influences the position of the spirometer bell.

When the apparatus has been set up with the bottles filled, attention should again be given to the direction of the inlet tubes in the Williams absorbers because an error in the position of these tubes will result in forcing acid out of the bottles into the metal or rubber parts of the apparatus. The three-way valve at the mouthpiece is then turned so as to close the circuit and the motor is started. During the first few minutes there will be a slight increase in the temperature of the air inside the circuit due to the addition of moisture to the concentrated sulphuric acid. A



Rear View of Universal Respiration Apparatus.

certain amount of this heat is lost by radiation to the surrounding air and soon the temperature of the air becomes quite constant and there is no volume change from this source. When the blower is started the spirometer bell is seen to jump downward a few millimeters and this indicates the development of a slight negative pressure in the spirometer which obtains until the pressure thruout the apparatus has been equalized.

After a few minutes the pointer should indicate a constant volume in the spirometer for a period of 2 or 3 minutes before the apparatus can be considered tight. In case of leakage the pointer will indicate a steady loss of volume. If the apparatus be new it is well to test every possible source of leakage. The spirometer itself can probably be considered tight, tho in case of doubt the inlet and outlet tubes can be plugged with rubber stoppers and pressure made on the bell with a 200 gram weight. Leakage will be indicated by a change in volume. The remainder of the connections can be easily tested by applying a lather made from soap and hot water with a shaving brush. After the apparatus has been thus carefully gone over one need only look at the couplings of the Williams absorbers and the soda lime bottles which are opened from time to time and occasionally develop leaks. Before filling the soda lime bottles, we have made it a practice to fasten the metal top, insert the rubber stopper, lather the joint around the rubber gasket and then test for leakage by stopping the outlet tube with the finger and blowing into the inlet tube. In case of leakage the top should be removed, given a quarter turn to the right, and the test repeated until the bottle is tight. In filling these bottles it is convenient to have a tin funnel made so that it will easily fit the opening in the top and reach an inch or more below it. Occasionally the wire with which the rubber hose is fastened to the couplings will cut thru and in case of difficulty it is well to test for leakage here. Sometimes a patient is found whose nose is not completely closed by the nose clip. A little lather placed over the nostrils will determine leakage at this point.

Measuring the O_2 (Oxygen).— The O_2 consumed by the patient may be measured in several ways. Because of the difficulty of beginning and ending a period at exactly the same phase of respiration any error inherent in one of these methods is far exceeded by the mechanical or technical error common to all of them.

The method of determining the exact beginning and end of each period is of such importance that it is worth while to go into some detail to make clear the sources of error. Theoretically it should be possible to turn the three-way valve at the end of a normal expiration and start the stop-watch at the same moment for the beginning of the period. It is very easy however, even after considerable experience, to turn the valve a little too soon. The timing of this valve can be checked by noting whether the spirometer level at the end of the first 2 or 3 expirations agrees approximately with the reading taken before the valve was turned. In case of failure to agree it is clear that had the watch been started with the valve an error would have been introduced.

When the patient is excitable or nervous the expiratory volume will often suddenly increase when the valve is turned so that a true spirometer level for a normal expiration is not obtained. In such a case normal expiratory volumes might not be reached for several moments after turning the valve.

As soon as the patient is connected with the closed circuit the addition of CO_2 and water vapor will increase the volume between the three-way valve and the absorption bottles. After 6 to 12 respiratory cycles this volume increment of from 40 to 80 c. c. remains constant except for variations introduced by the type of breathing which may amount to from 30 to 60 c. c. If the valve be turned off at any time the volume of circulating air will be diminished as the unabsorbed water vapor and carbon dioxid pass thru the absorption bottles. Because of the comparative constancy of this volume increase while the patient is connected with the machine, and the accuracy with which the exact end of expiration can be determined from the spirometer pointer, we have adopted a method of marking the periods which eliminates the inaccuracy due to the three-way valve while introducing a maximum error of from 30 to 60 c. c. due to variation in the type of breathing.

The valve is closed at the end of expiration and a period of 12 or more respiratory cycles allowed to elapse. By this time the breathing will have become regular. The stop-watch is then started and the spirometer level read at the end of a normal expiration to mark the beginning of the period. After 10 minutes the spirometer level is observed at the end of a normal expiration and the watch stopped at the same instant. This marks the end of the period. Oxygen is then added and the procedure repeated once or twice as may be desired. Ten minute periods will vary very little when the operator becomes skilled and the metabolism has reached the basal rate.

The method of measuring the O_2 will be somewhat different when the expired CO_2 is to be weighed. This arises from the fact that the amounts of O_2 and CO_2 must be obtained for exactly the same period of time and will be discussed later under CO_2 measurement.

The simplest method of measuring the O_2 is by difference in the spirometer readings. This limits the length of the period to 10 or 12 minutes in the average individual. Longer periods may be run by determining O_2 differences by weight. The small type of O_2 cylinders fitted with a reduction valve will weigh between 7 and 8 kilograms. A balance with a capacity of 10 kilograms and a sensitiveness of .02 grams will then determine O_2 differences of 10 grams or more, with an error of much less than 1 per cent. The gas supplied to us has been found over 99 per cent. pure O_2. A source of difficulty in this method is leakage at the point of attachment of the reduction valve. Gaskets of lead are probably most satisfactory but a fresh one must be used each time the valve is detached. In using this method the spirometer is filled to a mark, O_2 is added from time to time and again at the end of the period until the bell has reached the first level. The O_2 cylinder is first weighed after filling the spirometer and again at the end of the period when O_2 has been added to the original level. Multiplying the difference in weights by the volume of 1 gram of O_2, 0.699, gives the volume of O_2 consumed. This volume does not have to be corrected for temperature or pressure.

Oxygen may also be measured by means of a Bohr gas meter. In this case the bell is filled to the original level after the period by passing O_2 slowly thru the meter and the volume corrected for temperature and pressure. It is well first to pass the gas under water in order that addition of water vapor in the meter may not influence the volume. The meter should be calibrated by weighing from a cylinder the amount of gas passed thru it. The rate of delivery should be kept about constant.

Measuring the CO_2 (Carbon Dioxid).— In measuring the expired CO_2 it is necessary to begin and end each period by turning the three-way valve at the end of an average expiration. When the valve has been opened the height to which the spirometer rises for the first 2 or 3 expirations should be averaged to get the reading. At the end of the period the valve is turned when the pointer indicates the end of an average expiration. The soda lime bottle and the Williams absorber next to it are weighed together before and after the completion of the test. The difference in weight multiplied by the volume of a gram of CO_2 (Carbon Dioxid), 0.5087, gives the volume of CO_2 expired. This need not be corrected for temperature or pressure. The weight can only be considered accurate if the air reaching the soda lime bottle be absolutely dry. Failure of the Williams absorbers to take up all the water vapor from the incoming air can be detected by weighing the soda lime bottle and the sulphuric acid container next to it before and after running a 10 minute blank. Increase in weight indicates escape of moisture from the air drying system and is corrected by changing the sulphuric acid. Loss of weight after the same blank denotes failure of the sulphuric acid to take up all of the moisture given off by the soda lime and is corrected for in a similar manner.

Preparation of Patient.— In order to obtain what is known as the basal rate the factors of food absorption and muscular activity must be eliminated. This is done by making the determination before breakfast and after a preliminary half hour period of absolute quiet in the recumbent position. It is probably better to transfer the patient from his bed to the calorimeter bed with a minimum of muscular activity so that in general outpatient determinations are to be discouraged. Readings of consecutive periods, however, will very often check remarkably well even tho the patient has walked some little distance beforehand. A fall in the O_2 consumption probably means that the basal rate has not yet been reached. In case the non-protein respiratory quotient is to be obtained the bladder should be emptied and a specimen of urine collected over a measured period of time from before the test is begun till after it is finished. The patient is weighed to tenths of a kilogram and the height taken to the nearest centimeter before lying down.

Making the Test.— The preliminary period of rest having passed, the bed on which the patient is lying is wheeled in position next to the calorimeter, the motor started and the spirometer filled with oxygen to about the 7 liter mark. The mouthpiece is adjusted and the nose clip applied. When the spirometer level is constant and the temperature has been taken the valve is turned and a period of 12 to 15 respiratory cycles allowed to pass. Then at the end of an average expiration the watch is started and the reading taken. After 10 minutes the watch is stopped at the end of an average expiration, the spirometer level observed, and the temperature again noted. The time of the period, and the two volume and temperature readings are recorded, the spirometer refilled and the same procedure repeated twice. At the end of the third period the valve is turned off for the first time and the test is finished. If the amounts of O_2 consumed in 10 minutes do not check within about 100 c. c. it is advisable to run one or more extra periods.

Calculating the Results.— The calculation of the results is much facilitated by the use of logarithms. The total volume of O_2 consumed is obtained by adding the difference in the spirometer readings for each period. This volume is reduced to 760 mm. by multiplying by $\frac{\text{barometer}}{760}$ and to 0°C. by multiplying by $\frac{273}{273 + \text{average temperature C.}}$ Dividing by the total time of the three periods gives the O_2 consumed per minute and from this the hour of the 24 hour amount is obtained by multiplying by 60 or 1440. This is converted into calories by multiplying by the heat value of a liter of O_2 at the respiratory quotient found, or by 4.825 if the R. Q. is assumed to be .82. The further calculation will depend on whether the Du Bois standard or the Benedict standard is to be used. In the former case the body surface is determined by the Du Bois formula from the height and weight and the number of calories per square meter per hour found by dividing the calories per hour by the body surface. Dividing by the expected number of calories per square meter for the age and sex gives the relation to the normal, which is multiplied by 100 to get the per cent. of normal. If over 100 this is written as per cent. higher than the theoretical value;

if less than 100 the figure is subtracted from 100 and the difference written as per cent. below the theoretical value. A variation of 10% above or below the normal is allowed but in general variations up to 15% below or 25% above are considered significant only when taken in conjunction with clinical findings. If the Benedict standard is used the number of calories per 24 hours is divided by the expected number of calories at the height, weight, age and sex of the patient and the result expressed in per cent. as above.

Calculation of the respiratory quotient adds somewhat to the accuracy of the test as the heat value for 1 liter of oxygen varies slightly with it. The difference, however, is so slight that for clinical purposes it can be ignored and the heat value of a liter of O_2 taken at the average respiratory quotient of .82.

On theoretical grounds it is perhaps still more accurate to obtain the non-protein respiratory quotient as the heat values of O_2 at the different respiratory quotients are calculated on this basis. This also allows a computation of the relative amounts of protein, fat and carbohydrate burned in the organism during the period of the test.

The respiratory quotient is an expression of the relation of the carbon dioxid expired to the oxygen consumed ($\frac{CO_2}{O_2}$ = R. Q.) The weight of CO_2 absorbed is multiplied by 0.5087, the volume of a gram of CO_2, and the volume thus obtained divided by the corrected volume of O_2 consumed.

A part of the energy of protein burned in the body is lost in the urine by the excretion of substance which may be still further oxidized. The O_2 and the CO_2 values for these must then be subtracted from the theoretical amounts of O_2 and CO_2 for protein and the remainder considered available for respiratory exchange. It can be calculated that when protein is burned in the body, for every gram of N excreted in the urine 9.35 gms. of CO_2 will be given off and 8.45 gms. of O_2 absorbed for protein alone. The total N excreted in the urine during the period of the test having been calculated, the amounts of O_2 and CO_2 for protein are obtained by multiplying by 8.45 and 9.35 respectively and subtracted from the weight of O_2 consumed and CO_2 given off. The remaining O_2 and CO_2 are left for fat and carbohydrate and after converting to volume the relation between them is expressed as the non-protein respiratory quotient.

$$\frac{CO_2}{O_2} = \text{non-protein R. Q.}$$

The computation on page 265 is one made on a patient with exophthalmic goiter. The heat value of O_2 at the given respiratory quotient and the volumes of 1 gm. of O_2 and CO_2 are taken from Lusk[1] where a full discussion of the principles involved may be found. When the respiratory quotient is not desired the calculation is simplified by the omission of the first and third portions.

[1] Lusk, Graham: The Science of Nutrition, 641 pp., $6.50, W. B. Saunders Co., Philadelphia, Pa. 1917.

CHAPTER 9

THE JONES "METABOLIMETER"[1]

By Robert C. Lewis, Ph. D.

Principle of the Method.— The determination of the basal metabolic rate is made with the Jones "Metabolimeter" by measuring the time required for the patient to consume exactly 1 liter of oxygen under standard conditions of pressure (760 mm. of mercury) and temperature (0°C.). The apparatus is the closed circuit type in which it is necessary to measure only one gas, the oxygen, the assumption being made that the respiratory quotient of the patient is constant under conditions of the determination. If a rigid adherence to the rules for preparation of the patient (see chapter 3) has been made, the R. Q. (respiratory quotient) will closely approximate 0.82. The heat value of oxygen varies to a small degree with the respiratory quotient; with an R. Q. of 0.82 it has been shown to be 4.825 calories per liter. Using this value and the time required to consume 1 liter of oxygen, it becomes a very simple matter to calculate the amount of heat produced per hour and, by estimating the surface area of the patient from a height-weight chart (after Du Bois), the amount of heat produced in calories per hour per square meter of body surface may be determined. This latter figure is the basal metabolism.

Description of the Apparatus.— The metabolimeter consists essentially of (1) a CO_2 absorption tower connected on the one hand directly with (2) a flexible rubber bag and on the other with the patient's lungs by means of rubber tubing and a special mouthpiece, the nose being closed by a suitable clip. Connection is also made with (3) a measuring cylinder and this in turn with (4) an oxygen tank. All connections between these different parts are rendered air tight by means of rubber or threaded connections, the latter being provided with rubber washers.

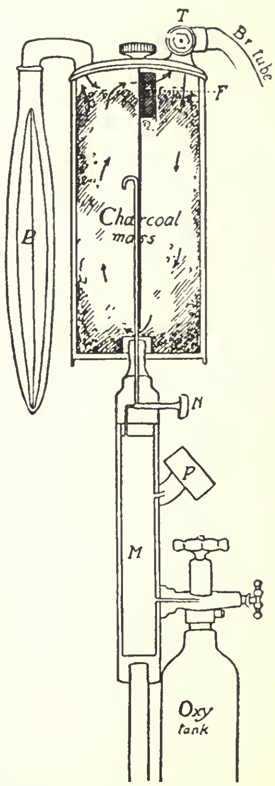
[1] Designed and described (Jour. Am. Med. Ass., **75**: 538, 1920,) by Dr. Horry M. Jones of the University of Illinois College of Medicine.

(1). The CO_2-absorption tower.—The CO_2-absorption tower is provided with a removable top which is held in place by a large hexagonal nut, and leakage at the cover is prevented by a rubber gasket. The tower is divided in the middle by a partition which runs from the top to within about 1 inch of the bottom. Near the top of this partition is a small opening provided with a flutter valve, which permits the passage of air in one direction but not in the other. The tower is filled with broken charcoal varying from the size of a pea to that of a small chestnut. The charcoal is kept saturated with fresh, strong sodium hydroxide solution.

The tower has 3 openings, 2 in the cover and 1 thru the bottom. As represented in the diagram the openings in the cover pass to the flexible rubber bag and the breathing tube, respectively. The opening in the bottom serves for the admission of oxygen from the measuring cylinder. This opening, instead of simply being tapped thru the bottom, is brought up to the center of one half of the tower by small metal tubing. This arrangement prevents sodium hydroxide solution from getting back into the measuring cylinder. As shown by the arrows in Fig. 2 (next page), air in passing from the patient's lungs is forced by the mechanical construction of the tower to pass down one side, under the partition, and up the other side, thus coming in contact with the large surface of sodium hydroxide on the pieces of charcoal and thereby losing its CO_2 before returning to the patient's lungs via the shorter route thru the flutter valve.

(2). The measuring cylinder.—The measuring cylinder is considerably smaller than the CO_2-absorption tower. It is provided with a pressure gage and is connected at the top by a needle valve with the CO_2-absorption tower, and at the side with an oxygen tank. The gage is so standardized that the measuring cylinder will deliver exactly 1 liter of dry oxygen under normal pressure (760 mm. of mercury) and normal temperature (O°C.), no matter what the room temperature may be. This is accomplished by having the gage marked in terms of degrees of temperature (Centigrade), the cylinder being filled with oxygen until the gage records a pressure corresponding to the room temperature mark. In other words, when the room temperature is 25°C. enough additional pressure is used over that provided for 15°C. to offset the expansion effect of the difference of 10 centigrade degrees in the volume of oxygen. In this way exactly 1 liter of gas measured directly in terms of 760mm. pressure and 0°C. is always used for a test.

(3). Flexible rubber bag.— The patient breathes back and forth into a closed, air tight apparatus, all parts of which are of fixt volume except the flexible rubber bag. This bag is directly connected with the CO_2-absorption tower by means of its rubber tubing neck and, as the patient expires and inspires into the closed system, the bag expands and contracts.



(4). Oxygen tank.— A small size oxygen tank (about 16 inches long and of 40 gallons capacity, obtainable from a supply house in any large city) fits in a clamp at the side of the measuring cylinder and has an air tight connection with it. No other kind than a round wheel-wrench (furnished with the metabolimeter) is satisfactory for use with this tank, for with it and with no other kind of wrench or key can one have perfect control over release of gas from the oxygen tank into the measuring cylinder. Overcharging the measuring cylinder will result in injury to the pressure gage, thereby rendering it inaccurate until re-calibrated (see paragraf on recalibration of pressure gage below).

Preparation of the Apparatus.— The apparatus is kept packed in a suitable carrying case, all parts except the oxygen tank being contained therein. The oxygen tank is obtained from a local dealer or one in a nearby city. The various parts are removed from the box and the metabolimeter is assembled as shown, care being taken to see that all threaded connections are provided with washers, thereby preventing leakage. The oxygen tank should hang directly over one foot of the tripod. If the apparatus is to be used for the first time, the charcoal is removed from the CO_2-absorption tower to a granite-ware or white enamel pan, covered with about 2 liters of 50 per cent. solution of sodium hydroxide, and allowed to stand over night. The excess of sodium hydroxide solution is then poured off and the CO_2-absorption tower is filled with the wet charcoal. Thereafter this moistened charcoal is kept in the CO_2-absorption tower, accumulated carbonates being washed out at the end of each series of tests by pouring 200 c. c. of water into the tower, allowing it to stand for a few minutes, and then replacing it with a second 200 c. c. of water. This water is allowed to remain in the tower until the apparatus is again needed, when it is poured off just before the metabolimeter is assembled. By this procedure the charcoal in the CO_2-absorption tower is kept moist and clean at all times.

Just before a test is to be made all fluid is removed from the CO_2-absorption tower, as noted above, and 100 c. c. of 50 per cent. sodium hydroxide is poured over the charcoal, care being taken to distribute the alkali evenly to each half of the tower and not to pour it on the flutter valve. The cover is then put in place with the breathing tube outlet (the one with the three-way cock) on the flutter valve side of the tower. The apparatus is now ready for the metabolism determination, if a test shows it to be gas tight.

To determine whether or not the apparatus leaks, the needle valve is closed and oxygen is cautiously admitted to the measuring cylinder by carefully turning the wheel wrench of the oxygen tank. When the indicator of the pressure gage is approximately at a point corresponding to the room temperature (in centigrade degrees), the outflow of gas from the oxygen tank is stopped and the needle valve of the measuring cylinder is opened. Gas escapes from the measuring cylinder into the CO_2-absorption tower and the rubber bag distends. When the side of the bag almost touches the tower, the needle valve is closed and oxygen is again admitted to the measuring cylinder until the indicator of the pressure gage registers, after tapping the gage with a finger, exactly at the point corresponding to the centigrade temperature. If the indicator has gone beyond the desired point, the excess of gas may be discharged by opening the needle valve. The measuring cylinder now contains a supply of oxygen such that, when the needle valve is opened, exactly 1 standard liter (if measured at 0°C. and 760 mm. of mercury) of oxygen will be discharged into the closed system of the metabolimeter. The extent of space between the bag and the CO_2-absorption tower is now carefully noted and the stop watch (provided with the apparatus) is run for 1 or 2 minutes. If at the end of this time no increase in the space has occurred and the pressure gage still reads to correspond with the room temperature, all parts of the apparatus (closed system and measuring cylinder) are gas tight and ready for a metabolic rate determination. If a leak has occurred, it should be diagnosed by the procedure given below (see paragraf on Location of Leaks).

Before being used the mouthpiece, noseclip and breathing tube should be sterilized. This may be done by boiling in water or by immersing in 50 per cent. alcohol. At the end of each series of tests these parts should be removed and thoroly washed under a water faucet before being sterilized for the next patient.

Preparation of the Patient.— The routine is given in Chapter 3. Above everything else, care must be taken to make the patient comfortable, raising the head on the bed by pillows if necessary. An explanation should be made to the patient that the only discomfort will be the slight inconvenience of breathing thru the mouth, and that all bad air is removed by the tower. The mouthpiece is connected with the apparatus in such a position that, when it is placed in the mouth, the breathing tube will not have to be rotated even to the slightest degree. The mouthpiece is inserted into the mouth, and the upper and lower lips pulled well out and over the shield to make an air tight connection. The nose must be made air tight without causing the patient any discomfort.

The Metabolism Test Proper.— After ascertaining again that the bag has not collapsed to an appreciable degree and that the indicator of the pressure gage still corresponds with the room temperature, the three-way cock is turned at such a time during expiration as to allow the last one third of the volume of air expired to enter the apparatus. The bag expands so as to touch the side of the tower and then falls away during inspiration. With each respiration some of the oxygen is consumed and, as the carbon dioxid expired is absorbed by the alkali in the tower. the volume of gas in the closed system (lungs, breathing tube, CO_2-absorption tower, and bag) decreases slowly. Finally there comes a time when the bag fails to touch the side of the tower at the end of expiration. This may be determined with ease by the use of a white background and should occur after 5 to 10 respirations. If too much of the expired air is admitted, an unnecessarily long time may elapse before the beginning point is reached; if too little, the bag may fail to touch the tower, thereby necessitating an entirely new start (refilling of bag and measuring cylinder). When the bag fails to touch the tower for the first time, the operator counts one; at the second failure, two; and finally, when the bag fails to touch for the third successive time, three. At this instant the stop watch is started and the measurement of the time required for the patient to consume 1 liter of oxygen has begun. The needle valve of the measuring cylinder is now opened slightly and the oxygen contained therein under pressure is allowed to escape slowly into the closed system. When the measuring cylinder has been completely discharged, as determined by the fact that the indicator of the pressure gage stands, after gentle tapping, at the zero pressure mark, the needle valve is again closed. Exactly 1 standard liter of oxygen has been admitted to the closed system and must be consumed before the rubber bag returns to its initial position.[2] In the same way as the beginning point was chosen, so the end of the period is taken as that time when the bag fails to touch the tower at the end of expiration for the third successive time. At this instant the stop watch is stopped, the three-way cock is turned, the mouthpiece and noseclip are removed, and the patient is allowed to rest for a few minutes. The stop watch is then carefully read and the time noted (in minutes and hundredths thereof). An error in reading of 1 minute is not unusual for one who is not thoroly accustomed to a stop watch; so that extreme

[2] Even if the oxygen used is not absolutely 100 per cent. pure, 1 standard liter of oxygen must be consumed before the rubber bag will return to the beginning point, oxygen previously present in the closed system being used in place of the inert gas which has been discharged.

care should be taken to prevent an erroneous conclusion as a result of inaccurate reading of the time.

In our experience (at the Laboratories of the Medical and Surgical Group of Denver) it is not necessary to remove the tower and replace the alkali until 2 determinations have been made. Consequently, after the patient has rested for 5 minutes the mouthpiece and noseclip are again put in place and the test is repeated as described above. If the time required to consume 1 standard liter of oxygen checks the first test within 0.2 of a minute, it is not necessary to proceed further. However, the first test generally gives erroneous results, probably due to the nervousness of the patient, and must be discarded. In this event a third test must be made. Before doing this the CO_2-absorption tower is removed and the alkali is poured off from the side opposite the flutter valve. A square of wire gauze with a hole punched in the center facilities removal of the alkli without loss of charcoal. A fresh 100 c. c. portion of 50 per cent. sodium hydroxide (sufficient for 2 additional determinations) is then poured over the charcoal, the apparatus is again assembled and a third test is made. If, as occasionally happens, checks are not obtained, additional determinations are made until it is established beyond the shadow of a doubt what time is required for consumption of a standard liter of oxygen under basal conditions. Unless close checks are obtained, entirely erroneous conclusions may be drawn as to the actual basal metabolic rate of the patient.

Altho the data is not needed for calculation of results, valuable information for aid in diagnosis to be used along with the figure for basal metabolic rate, may be obtained by noting the pulse and respiration rates. The former should be taken between tests, the latter by counting the number of excursions of the flexible rubber bag during the third minute of the test.

After the tests have been completed the patient's height (stocking feet) in inches should be measured and the weight in pounds taken. For the purpose of calculation, nude weight is required, and may be calculated sufficiently accurately by subtracting the approximate weight of the clothing from the weight of the patient as taken. The age of the patient must also be ascertained.

Calculation of Results.—Having obtained checks on the time required for the consumption of 1 liter of oxygen, the average of these figures is taken as a basis for the calculation of the basal metabolic rate. It should be remembered that the quantity of oxygen consumed during a test would equal exactly 1 liter measured under standard conditions (at a barometric pressure of 760 mm. of mercury and a temperature of 0°C.). Consequently, it is not necessary to correct the oxygen consumption to standard conditions, as would be required with any other type of apparatus; the oxygen consumed during each test is exactly 1 standard liter, no matter under what condition of atmospheric pressure and temperature the test may have been conducted.

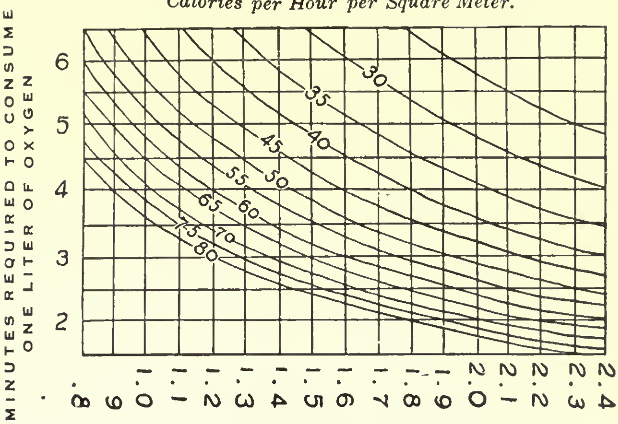
Knowing the time required to consume 1 standard liter of oxygen, the consumption per hour may be readily calculated. By dividing this figure by the body surface the oxygen requirement per square meter of body surface is obtained. If the assumption is made that the respiratory quotient is 0.82, each liter of oxygen will yield 4.825 calories (see paragraf on Principle of the Method). By multiplying the figure for oxygen consumption per square meter of body surface by 4.825, the basal metabolism, i.e., the heat production in calories per hour per square meter of body surface, is obtained.

In actual practice all figuring is eliminated by the use of charts provided with the apparatus. From the Body Surface Chart and Tables in Chapter 28 the body surface in square meters may be quickly obtained from the data of weight and height of the patient. The body surface area is used with the average time obtained for the consumption of 1 standard liter of oxygen for finding from Table 2 the basal metabolism of the patient. The intersection of the "body surface" and "time" lines is noted and its position between the oblique lines for basal metabolism is estimated to within 0.5 of a calorie. What the basal metabolic rate of a normal person of the age and sex of the patient should be is found in Table 3. The plus or minus per cent. rate is found by using the figures for the normal rate and observed rate in Table 4. The intersection of the lines for these two rates is noted and the plus or minus rate is read off from the oblique lines by interpolation, just as was done with the other charts. Thus the complete calculation of results is made by the reading of charts.

To give a concrete example of a calculation: Female, age 32;

TABLE 2

For Reducing Stop-watch Time and Patient's Body Area to Calories per Hour per Square Meter.



Curved lines = calories per hr. per sq. meter

TABLE 3

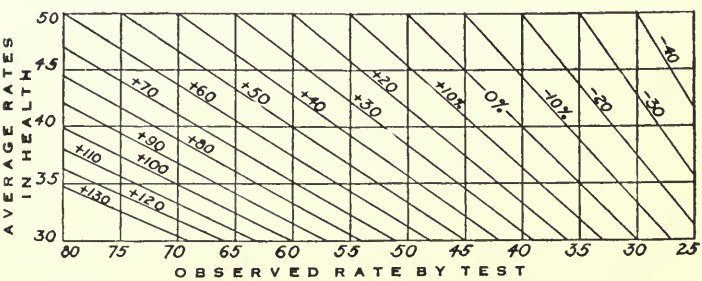
Average Rates of Persons in Health, in Calories per Hour per Square Meter Body Area

(From Aub and DuBois)

Age	Males	Females
6–8	58.0	58.0
8-10	54.0	54.0
10-12	52.0	50.0
12–14	50.0	46.0
14-16	46.0	43.0
16-18	43.0	40.0
18-20	41.0	38.0
20-30	39.5	37.5
30–40	39.5	36.5
40-50	38.5	36.0
50-60	37.5	35.0
60–70	36.5	34.0
70-80	35.5	33.0

TABLE 4

For Reducing Patient's Calories per Hour per Square Meter to plus or minus Per Cent Rate of Metabolism



Radiating lines = plus or minus % rate, considering average rate in health as zero%, height 64 inches; weight (corrected for clothing), 135 lbs.; average time to consume 1 standard liter of oxygen, 4.53 minutes. From Tables, or Body Surface Chart in Chapter 28, the weight and height values indicate a body surface area of 1.66 square meters. From Table 2 the body area line (1.66) and average time line (4.53) intersect at a point between 35 and 40, estimated as 38. Table 3 shows the normal rate of a female, age 32, to be 36.5. From Table 4 it is found that the observed rate line (38) intersects the normal rate line (36.5) at a point just below the 0 per cent. oblique line. The rate is estimated to be +4 per cent.

Sources of Error.— With any basal metabolism determination, no matter what apparatus is used, one must be ever watchful to prevent the creeping in of errors. The sources of error to which determinations with the metabolimeter are subject fall under 3 headings: those due to (1) the patient, (2) the apparatus, (3) the operator. Lack of space prevents a detailed discussion of these various sources of error, prevention of which must be assured if reliable determinations are to result. However, the most common may be advantageously listed as follows:

1. Failure of patient to refrain from eating for 14 to 16 hours.
2. Failure of patient to remain quiet thruout 30 minute preliminary period and tests.
3. Irregular breathing of patient, if occurring near beginning or end of a determination. (After patient becomes accustomed to the test no trouble in this respect is usually experienced.)
4. Leaks in the apparatus, thru nose or around mouthpiece. (A test for leakage of the apparatus should be made a preliminary to each new series of tests.)
5. Dirty apparatus with resultant sticking of flutter valve or clogging of the CO_2-absorption tower with carbonates. (Avoided if directions for cleaning apparatus are followed after each test.)
6. Inaccurate pressure gage. (Should be recalibrated from time to time.)
7. Too much fluid in apparatus. (Due in every case to faulty technic.)
8. Incorrect position of top of CO_2-absorption tower. (Breathing tube outlet should be on flutter valve side.)
9. Incomplete absorption of CO_2. (Avoided if directions as given are followed.)
10. Inaccurate filling of measuring cylinder.

11. Inaccurate reading of stop watch.

12. Inaccurate reading of charts in the calculation of results.

13. Inaccurate weight and height figures. (One should never guess; patient should always be weighed and measured.)

14. Failure to get tests to duplicate one another. (Readings should agree within 2 per cent. of their average.)

If care is taken to avoid the errors from these various sources, no trouble will be experienced in getting dependable results with the metabolimeter.

Location of Leaks.— As noted before, a test for leaks in the apparatus should be made a preliminary of each new series of tests. The method of making such a test has already been described (page 107). In case there results a perceptible increase in the space between the CO_2-absorption tower and the flexible rubber bag, the conclusion may be drawn that the bag has collapsed as a result of a leak in the closed system of the apparatus. The most probable sources of such a leak are around the top of the CO_2-absorption tower on account of a dirty rubber gasket, at the bottom of the tower, or in the three-way valve of the cover. Such leaks may be prevented by cleaning the rubber gasket, by putting a new rubber washer in the connection between the $CO\text{-}_2$absorption tower and the measuring cylinder, and by tightening the nut on the three-way cock. After the apparatus is again assembled the test for leakage should be repeated to insure that the desired correction has been made.

If the indicator of the pressure gage recedes after the measuring cylinder is filled, even tho the needle valve is closed, a leak is occurring in this part of the apparatus. The most common causes of such a leak in the measuring cylinder are the valve of the oxygen tank and the connection between the oxygen tank and the measuring cylinder. If the leak still occurs after a new washer is put in this connection, the oxygen tank valve is probably at fault. To confirm this suspicion, the CO_2-absorption tower should be removed, the rest of the apparatus turned upside down, and the end of the oxygen tank valve immersed in a beaker or glass of water. Escaping bubbles show the leak to be along the stem of the oxygen tank. If this can not be remedied by moderate tightening of the top nut of the oxygen valve, a new tank should be secured.

Leaks thru the nose can be avoided by careful adjustment of the noseclip and subsequent testing of its tightness by having the patient attempt to force air thru the nose.

Occasionally the rubber shield of the mouthpiece gets so that it fits the metal part too loosely. If this happens, a new rubber shield should be substituted for the old, or adhesive tape may be used to insure a tight connection between the rubber and metal parts of the mouthpiece.

The best assurance that no leaks are occurring is the ability to obtain duplicate determinations with the metabolimeter. This is obviously impossible if one is not working with a gas-tight system.

Recalibration of the Measuring Cylinder. As the correctness of the basal metabolic rate determination depends very largely upon the accuracy of the pressure gage, the measuring cylinder must be recalibrated from time to time. As a routine this should be at least once a year; more if the gage should become overstrained by the too sudden release of gas from the oxygen tank. Recalibration is accomplished by filling the measuring cylinder so that the indicator of the pressure gage corresponds to the room temperature, collecting the gas discharged under water, and measuring it to see if the correct volume has been delivered.

The apparatus is set up as usual for making a test except that the CO_2-absorption tower is left off. In its place is screwed a small gooseneck connection (this may be purchased from the manufacturers of the metabolimeter) to which a small rubber tubing 2 to 3 feet in length has been attacht. To insure that this connection is tight the whole apparatus is inverted and the gooseneck connection is immersed in a large bucket (2 or more gallons capacity.) If no bubbles appear when one blows thru the rubber tubing, it may be concluded that the gooseneck connection is gas tight.

The next step is to calculate what the volume of a standard liter of gas at 0°C. (and 760 mm. pressure) will be under the conditions of temperature and pressure at the time of the test. The water used in the test should be kept at 23°C. At this temperature the liter would increase in volume to $\frac{296}{273} \times 1000 =$ 1084 c. c., provided the barometric pressure was 760 mm. of mercury. The volume at any other barometric pressure may be found by the following formula:

$$X = 1084 \times \frac{760}{\text{Barometric pressure -22 mm}}$$

where X is the volume at the barometric pressure under which the test is conducted and the 22 mm. is a correction for the aqueous tension at 23° C. For example, with a barometric pressure of 622 mm. (about the average for Denver) this formula works out as follows:

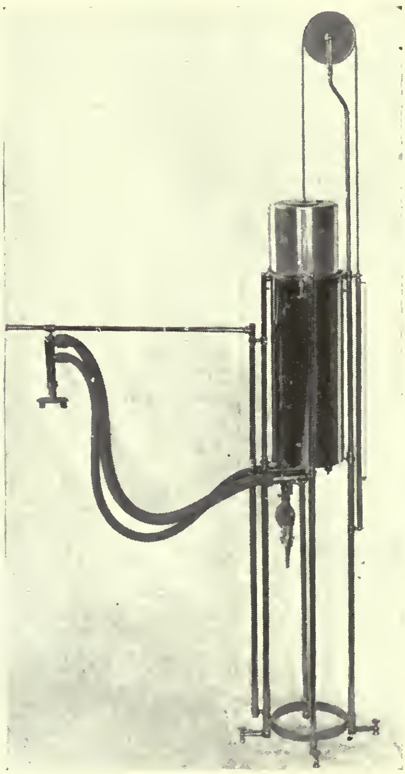
$$X = 1084 \times \frac{760}{600 \quad \text{(i.e. 622 - 22)}} = 1373 \text{ c.c.}$$

Having ascertained what the volume of a standard liter will be under the condition of the test, a liter volumetric flask and a graduated cylinder (200 to 500 c. c., depending on the volume required to provide for 1 standard liter of oxygen after release from the measuring cylinder) are filled with water and placed bottom upward in a bucket of water kept at 23° C. The needle valve of the measuring cylinder is closed and oxygen is run in from the oxygen tank until the pressure gage reads to correspond with the room temperature. The gas is then discharged slowly into the volumetric flask by placing the rubber tubing well up into the flask and opening the needle valve of the measuring cylinder. When the gas has almost displaced 1 liter of water, the rubber tubing should be drawn down below the liter mark and the last few c. c. of oxygen should be run in while this mark is on a level with the water in the bucket. In a similar manner oxygen is run into the graduated cylinder until the volume which 1 standard liter of gas will measure under conditions of the test has been reached. The pressure gage is then tapped, its front is unscrewed, and a fine pencil mark is made beneath the indicator point to denote the correct zero-pressure mark. If no more oxygen is released from the tank when the needle valve is opened, the measuring cylinder is delivering exactly a standard liter. In case more gas than the liter is discharged, the indicator hand of the pressure gage must be set to correspond to the zero pressure mark previously made. This is done with a special tool provided with the calibrating equipment. If the measuring cylinder has failed to deliver a standard liter, the indicator hand of the gage must be moved a short distance counter-clockwise and the recalibrating procedure repeated as just described. By such recalibration the accuracy of the metabolimeter may be insured at all times.

CHAPTER 10

THE COLLINS BENEDICT APPARATUS[1]

Description of the Apparatus.— This is a simple, portable apparatus for measuring the consumption of oxygen, by which may be determined the basal metabolism of a subject. A general view of the apparatus, and also a sectional diagram of it, are shown below:



APPARATUS READY FOR USE

[1] Editor's abstract of "A Clinical Apparatus for Measuring Basal Metabolism," by F. G. Benedict and W. E. Collins, Boston, Med. and Surg. Journ. Oct. 14, 1920.

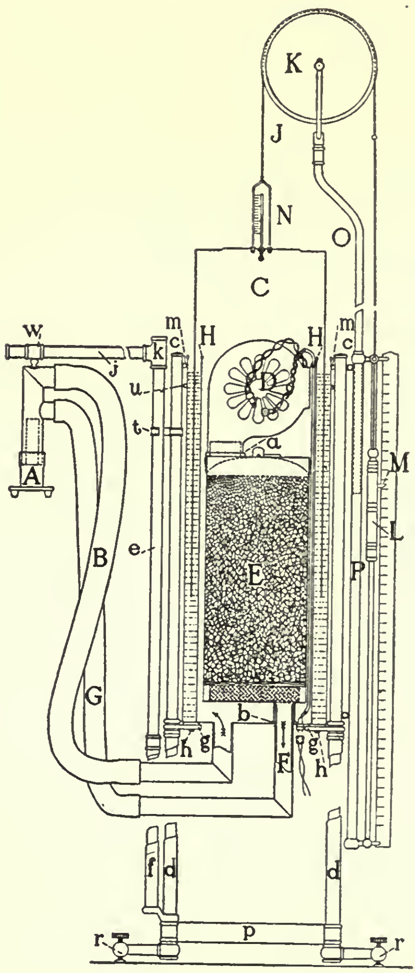
The general view shows the apparatus as it is used at the bedside. It may be made ready for carrying about by depressing the oxygen bell, telescoping the legs of the frame, the horizontal arm, and the upright for the pulley. Inside of the apparatus are the electric fan, and the soda lime for absorbing the carbon dioxid. These parts are shown in the sectional diagram.

The mechanical blower, or fan, which is placed inside of the spirometer, was originally designed for a hair dryer. This hair dryer is substantially made, with a cast aluminum housing, and for use in this apparatus is divested of heat unit, handle and switch, and otherwise slightly modified. The object of the fan is to force the air thru the soda lime and thus deprive it of carbon dioxid and send it in respirable condition to the mouth.

The soda lime is also inside the spirometer in a metal can. In the bottom of the can is an opening somewhat off centre which fits exactly over the discharge pipe from the spirometer leading the air to the mouth. The top of the can is removable and likewise has an opening set off centre sufficiently to take the discharge opening of the fan. An interior screen and layers of cheese cloth in the bottom of the can prevent the discharge of dust from the soda lime. While under ordinary conditions it is absolutely essential to have soda lime fairly moist to absorb carbon dioxid to its greatest efficiency, in this particular type of apparatus, where the air enters the soda lime moistened from the lungs, almost any kind of soda lime will do. To keep the cap in place, a good, stout rubber band is snapped around it. Where the can fits over the pipe in the bottom of the spirometer, it rests against a rubber ring washer, thus making a reasonably tight closure. A gasket is used where the hair dryer is attached at the top.

A rubber tube, ⅝ inch internal diameter, brings the air from the blower to a light metallic pipe to which the rubber mouthpiece is attached and the air is returned to the spirometer in a rubber tube 1 inch inside diameter. The stem of the rubber mouthpiece ordinarily used is long enough to be grasped by the thumb and finger to cut off the air current momentarily while filling up with oxygen. This stem can likewise be collapsed by a large spring clamp.

Testing the Apparatus.— The testing of the ventilating conditions existing in the soda lime can is fortunately very easily carried out, and should be frequently made. With the motor



Respiration Apparatus. *A,* mouthpiece; *B,* tube conducting expired air to bell *C; D,* hair dryer; *E,* soda-lime container; *F* and *G,* tubes conveying air current to mouthpiece *A; HH,* tank in which bell *C* floats; *J* and *K,* cord and pulley supporting bell *C; L,* counterpoise; *M,* pointer on counterpoise; *N,* thermometer; *O* and *P,* supports for pulley *K. a,* rubber gasket; *b,* rubber gasket; *c, c,* tubes supporting spirometer; *d, d,* lower part of frame supporting spirometer; *e* and *f,* telescoping tubes supporting mouthpiece and tubing; *g, g,* supporting plates; *h, h,* knobs fitting into *g, g; jk,* part of support for mouthpiece and tubing; *mm,* attachment to support *c, c,* to tank *HH; p,* circular band connecting four tubes, *d, d; r, r,* levelling screws; *t,* sliding ring; *u,* knobs for support of apparatus when collapsed; *w,* sliding ring.

running, the bell filled with air, and the thumb over the mouthpiece, an assistant at a given signal forcibly collapses the air pipe leading from the mouthpiece to the spirometer, *i. e.*, the larger of the two rubber tubings. At the same instant the thumb is removed from the mouthpiece, the bell instantly starts to descend, and the length of time it requires to make a complete descent is noted. These bells should travel over a distance corresponding to not far from 9 liters and, consequently, 9 liters in 20 seconds or less is ample ventilation. Indeed, there is a certain disadvantage in having too high a ventilation, primarily on account of the fact that the less current passing thru the motor, the greater the factor of safety in case of accident, stoppage of motor, with building up of current, burning out of resistance, and combustion in an oxygen-rich atmosphere.

As a result of a great deal of experience in the laboratory it has been deemed desirable that the air crurent in any of the several types of closed circuit apparatus should ventilate not less than 25 liters per minute by the mouthpiece to prevent rebreathing. The hair dryer will discharge a very large volume of free air and consequently it is necessary to cut down the rate of discharge by external electrical resistance, usually a 120-watt lamp directly in series, and even under these conditions, with ordinary soda lime, no difficulty is experienced in getting a delivery of 60 liters of air.

Making the Test.— The method of use of this type of apparatus may be briefly summarized as follows:

Half-hour period of complete repose on the part of the subject.

Attach stethoscope for pulse and record pulse during repose.

Oil blower and run it a moment or two before putting bell in place.

Test ventilating rate, as outlined in text.

Insert mouthpiece, shutting off connection to apparatus by fingers or by clip.

Fill apparatus with pure oxygen, starting from bell at lowest point.

Start blower.

Remove clip, connecting mouthpiece to apparatus and attach nose-clip.

When respiration is regular take three initial readings of spirometer counterpoise position, temperature of bell, and exact times.

Read thermometer in bell.

After about 8 or 9 minutes repeat series of readings of spirometer position, temperature of air in bell, and time.

Take off nose-clip, stop motor, remove mouthpiece.

Method of Recording Data.— A simple and most satisfactory method for recording data has been worked out as follows: The operator uses his ordinary watch, on which, however, care has been taken to set the minute hand to agree reasonably well with the second hand. After the subject is connected with the respiration apparatus, the nose-clip applied and the respiration has become regular (within a few seconds) the operator notes the position of the pointer on the counterpoise at the end of three or four successive exhalations. Due to the continual absorption of oxygen the bell should fall slightly during each respiration, and consequently the counterpoise pointer steadily, tho slightly, rises each time. The operator then immediately writes a final reading, for example 378 mm., on a pad or tablet and, *after he has written this*, he instantly notes the positions of the minute and hour hands. While the reading of the scale of 378 mm. may not occur at, for example, the recorded 8 hours 58 minutes 23 seconds, but, more strictly speaking, did occur more nearly 8 hours 58 minutes 13 seconds, owing to the latency of the time required to write down the figures, 378 mm. and 23 seconds, nevertheless we have found that the latency is practically the same for all records, and since the periods are always from 9 to 14 minutes long and essentially the same degree of latency is noted at the beginning and end of each set of readings, no error is thereby introduced. This method has other distinct advantages in that one can in the final computations note the drop in the spirometer bell between the first and the last reading at the end of the test, or can make any arbitrary combination of readings for computation purposes. Thus one can use the two outside or first and last readings, to give the longest period of experimenting, and the two inside readings to give the shortest, and note if there is any material difference between short and long experiments.

Calculating the Metabolic Rate.— The difference in the spirometer bell readings at the beginning and end of the test period is assumed to be the contraction in volume of oxygen, or the amount consumed by patient. The temperature in the spirometer bell read at the beginning and end of the test is averaged, the barometer is recorded and this contraction in volume reduced to 0°C. and 760 mm. by the usual method. Then a small empirical correction of 1 c.c. per minute for each degree rise in temperature of the bell is applied.

Benedict[1] states that "by means of indirect calorimetry it is possible to compute the calories of energy by using the measurement of the oxygen consumption. Zuntz has computed that each liter of oxygen consumed corresponds to a definite heat output, there being no great difference in this relationship whether the oxygen is consumed in burning carbohydrates (5.047 calories per liter) or fat (4.686 calories per liter). For practically all purposes, especially for clinical work, one may assume that the average respiratory quotient is 4.82. The calorific value of oxygen at this respiratory quotient is 4.825 calories per liter and 3.3777 calories per gram. Consequently, it is necessary only to multiply the liters of oxygen measured by 4.825 to compute the heat output."

Summary.— To fill urgent clinical needs the portable respiration apparatus has been modified, reduced in weight, and provided with support and stand so as to make is a strictly portable apparatus. Without gas analysis, without weighing of any kind, the oxygen consumption of patients may be studied by this apparatus in the customary 10 to 15 minute periods, wth an accuracy fully equal to other standard methods of studying respiratory exchange. A simple method of timing the readings of the position of the spirometer bell eliminates the use of stop watches. Three series of comparison tests on two different subjects with widely varying basal oxygen requirements show that the most satisfactory results can be obtained.

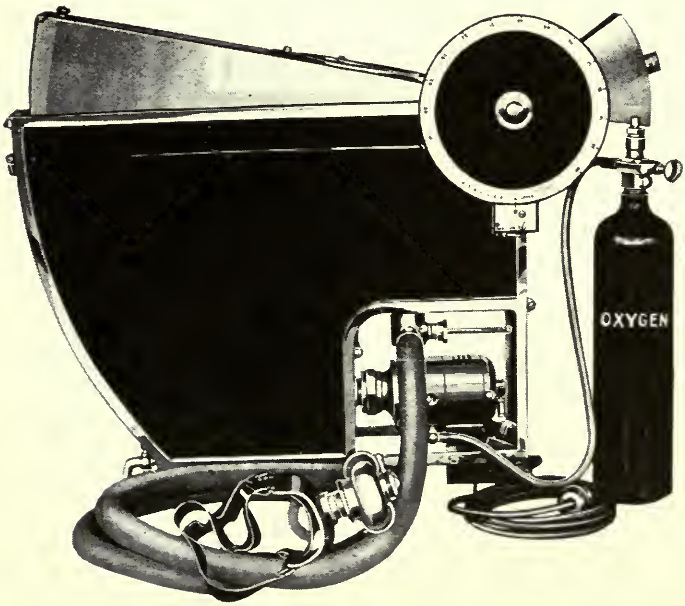
[1] Benedict, F. G.: A Portable Respiration Apparatus for Clinical Use — Boston Med. and Surg. Jour., May 16, 1918.

CHAPTER 11

THE "METABOLOR"

By Howard D. Haskins, M.D.

Description of Apparatus.— About a year ago Dr. McKesson of Toledo, Ohio, brought out a new apparatus for basal metabolism determinations under the name of "Metabolor". The technic for its use is practically the same as for the use of the Benedict apparatus. The metabolor is easily carried about, even without the case, since it is only 17 inches high and weighs about 40 pounds. It is very compactly built.



1921 Type of Apparatus with Direct Reading Dial.

It has a blower, the motor being placed outside in the lower corner of the apparatus. The absorber, an open box of soda lime, is placed inside the air chamber. The "float" (gas tank) is unique. This is fastened at one end with a hinge and is balanced by a heavy counterpoising weight. When oxygen is admitted to the tank, the free end rises so that the side wall of the tank shows a triangular surface. On the face of the free-moving curved end is a nickel-plated scale having a mark for each 25c. c. of volume. The readings are made opposite a fixed metal pointer. We have tested the scale and find it sufficiently accurate.

The inhaler is connected with the apparatus by means of two large flexible rubber tubes, 4 feet long, that have tapered metal ends which slip into place (near the motor) making air-tight joints, and being quickly connected or disconnected. The wire incorporated in the rubber prevents kinking or collapsing of the tubes. Because of this flexible connection there is no difficulty in adjusting the inhaler to the patient.

Preparation of the Apparatus.— Set it on a table in the proper position so that it will not need to be moved later on. Fill the water tank to the groove (12 liters) with water at room temperature. Test the balancing of the float by holding it so that it contains about 4 liters of air and then releasing it. If the tank is not in equilibrium, move the counterpoising weight until there is practically a balance (the tank may move but very slowly on being released).

Now, get the absorber ready. Two and a half pounds of soda lime are furnished with the apparatus, the entire quantity being used for the estimations. It is advisable to keep on hand a reserve stock of at least 5 pounds (it must not be coarser than 4 mesh). When the soda lime is first used sift out all the powdered material. Pour it into the special copper box, raise the air tank and slide the box into place (it telescopes snugly). The bottom of the box being wire gauze allows air to be sucked through the soda lime when the blower is working.

Wash out the rubber tubes, oil the metal joints slightly and connect with the apparatus. Oil the motor. Set the float so that it contains about 2 liters of air and turn the valve of the inhaler "off"; the system is now closed. Attach the oxygen tank to the little cock on one of the tubes and let the gas flow in very slowly until the apparatus contains about 7 liters, close the pet cock. Run the motor for a minute, or until the temperature is constant, and read the volume of the air-oxygen mixture.

Testing the Apparatus.— The apparatus may be tested for leaks at this point (it should be tested at least once each day) by putting a weight of about 100 grams on the high end of the float. After 10 minutes, run the motor for a minute, remove the weight and read the volume. This will be the same as the original volume if there has been no change in the temperature. This test can be carried out while the patient is resting.

Making the Test.— The patient has been prepared for the test by fasting and by a 30 minute rest period as fully described in Chapter 3. The rubber mouth piece, after being thoroughly disinfected and washed, is fitted to the inhaler and then inserted into the patient's mouth. The soft rubber bar is held between the teeth and the flap fits between the gums and the lips, exactly as with Benedict's inhaler. The special rubber "mouth-cover" and elastic head-bands furnished with the inhaler should be used whenever there is the least suspicion that the lips do not fit the inhaler air-tight.

Apply the nose clip, making sure that breathing through the nostrils does not occur. The patient is now breathing the air of the room through the inhaler (the valve being still turned to "off"). Start the blower. Note the volume and temperature of the oxygen mixture. When the patient is quiet and respiration is perfectly natural, turn the valve to "on", exactly at the end of expiration. He now breathes from and expires into the apparatus. Start a stop watch at the instant the valve is turned. The period of the test should be at least 10 minutes and not over 15 minutes. It seems to us advisable always to take an "inside period" also, which is done as follows. Watch the excursions of the float. When respiration is regular and is practically uniform in depth, at about 2 minutes after the start of the test, simultaneously read the volume at the end of an expiration and note the time (do not stop the watch). Read the thermometer at once. After 8 to 10 minutes more have elapsed when respiration is uniform, at the end of expiration read the volume and time simultaneously, then note the temperature. Read the barometer. You have now all the data for calculation of the metabolic rate on the basis of the inside period, the difference between the two volume readings giving the amount of oxygen used, and the difference between the time readings giving the minutes duration of the test.

The pulse and respiration rates should be taken several times during the test. If at any time the patient's breathing becomes irregular, shallower or deeper than ordinary, he should be warned to breathe more naturally.

When near the end of the time interval planned for the main test period (or sooner if the volume of air is approaching 2 liters, as may happen with a high metabolic rate) stop the test whenever respiration is most nearly uniform by turning the inhaler valve at the end of expiration and simultaneously stopping the watch. With the motor still running watch the float, and when the volume is constant make the reading. Note the temperature at once. Stop the motor and release the patient. It would be well to keep the patient recumbent until the calculations have been made, since it may be desirable to run a second test.

Calculating the Metabolic Rate.— Calculate the basal metabolic rate for both the main period and the inside period. The c.c. of oxygen consumed are found by deducting the final volume from the initial volume. The time is expressed as minutes and a decimal fraction. The mean between the two temperature readings is used for calculation. In the special table on page 129 look up the factor for correcting the oxygen volume for both temperature and barometric pressure (in one operation). With the aid of the curves on the chart (page 245) find the square meters of body surface at the point where the lines for the patient's weight (without coat) and height intersect. (Or instead of chart the Body-Surface Table on page 246 may be used. — Ed.).

c.c. $O_2 \times$ factor $\div$ minutes $\div$ sq.m. $= Z$, the c.c. of O_2 consumed per minute per sq.m. body surface

The per cent. of normal may be figured directly from Z by dividing it by the normal for the same age and sex, as shown in special table below, and multiplying by 100.

The further calculation for the basal metabolic rate is as follows:

$\frac{Z}{1000}$ 60×4.825, or condensed to $0.2895\ Z$ gives the calories per hour per square meter body surface. This divided by the normal found in the above table of metabolic rates and multiplied by 100 yields the figure for per cent. of normal.

AVERAGE NORMAL CONSUMPTION OF OXYGEN PER SQUARE METER OF BODY SURFACE IN C.C. PER MINUTE (AT 0°C. AND 760 MM.)

Ages	*Males*	*Females*
12-13	172	—
14-16	159	148
16-18	148	138
18-20	142	131
20-30	136	128
30-40	136	126
40-50	133	124
50-60	129	121
60-70	126	117
70-80	122	114

The main period and the inside period should agree within about 3%; if they do, take the average of the rates for the two periods. If the patient was nervous during the first few minutes, or if the expiration at the beginning of the test was less or more than natural, there will be considerable error in the results of the main period, and the rate will disagree with that calculated from the inside period. In this case it is advisable to run another test as soon as the patient is rested from the first test.

Notes. — 1. Benedict determined experimentally that under the conditions of the test the respiratory quotient is 0.82 which indicated a calorie value of 4.825 for each liter of oxygen consumed. Boothby states that the respiratory quotient is 0.84, (no data given), corresponding to 4.85 calories. The directions furnished with the metabolor use Boothby's figures. In our laboratory we prefer, however, to use Benedict's (as in formula above).

2. A modification of the metabolor is obtainable now. This has a dial giving direct readings of the oxygen used. The apparatus is also used for determination of "vital capacity" and of "ventilation rate". Either type of metabolor can be used to great advantage for administration of oxygen (as in pneumonia) since the amount actually consumed by the patient can be observed.

3. A face mask is furnished, this is used as an inhaler when oxygen is given therapeutically. The statement is made that it can also be used for the basal metabolism test. This is a doubtful proposition. It is difficult to get an air-tight fit of the mask to the face. If it is used apply vaseline quite freely, "puttying" the junction of the pneumatic pad with the skin. The mask should be closely watched thruout the test. It should be used only when the regular inhaler can not be used.

4. The motor is sure to give a proper circulation of the air in the apparatus if it is running at the accustomed speed (and if the soda lime is in proper condition) since the fan is so well constructed that it can not get out of order. Quick absorption (see note 5) is evidence that the motor is efficient. Eight liters of air will be drawn out of the tank in less than 10 seconds if one of the rubber breathing tubes is left disconnected; if both tubes are attached over 30 seconds is required.

5. The efficiency of the soda lime is indicated by the time required to bring the air in the tank to constant volume at the end of the test. When the soda lime is fresh it takes only 20 to 30 seconds. Discard the absorber when it takes over a minute. The soda lime should not become matted together or packed so densely that air can not be easily sucked through it. Pour it out of the box occasionally and examine its physical condition.

If left constantly in the apparatus too much moisture may be taken up. This can be avoided largely by plugging the top of the absorber box with absorbent cotton when the apparatus is not in use. When the float is lifted, be careful to avoid dripping of water into the soda lime. Another plan would be to lift the box out of the apparatus and keep it in a tightly closed box; or the soda lime may be transferred to the bottle.

6. Draw the water off before moving the metabolor.

Concluding Word.— We are confident that the metabolor will give exactly the same type of results as the standard Benedict apparatus.

FACTOR FOR CORRECTING VOLUME

TEMPERATURE CENTIGRADE

Barometer, Millimeters / Barometer, Inches

M.M.	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	*Inch*
720	.898	.894	.891	.888	.885	.882	.880	.877	.873	.870	.867	.864	.861	.859	.856	.853	.850	.848	.845	28.35
725	.904	.900	.897	.894	.891	.888	.886	.882	.879	.876	.873	.870	.867	.865	.862	.859	.856	.854	.851	28.54
730	.910	.907	.904	.901	.897	.894	.891	.888	.885	.882	.879	.876	.873	.870	.867	.865	.862	.859	.857	28.74
735	.916	.913	.910	.907	.904	.901	.898	.895	.891	.888	.885	.882	.879	.876	.873	.871	.868	.865	.863	28.94
740	.922	.919	.916	.913	.910	.907	.904	.901	.897	.894	.891	.888	.885	.882	.879	.876	.873	.870	.868	29.13
745	.928	.925	.922	.919	.916	.913	.910	.907	.904	.901	.897	.895	.892	.889	.886	.882	.880	.877	.874	29.33
750	.935	.932	.928	.925	.922	.919	.916	.913	.910	.907	.904	.901	.898	.895	.892	.889	.886	.883	.880	29.53
755	.941	.938	.935	.932	.928	.925	.922	.919	.916	.913	.910	.907	.904	.901	.898	.895	.892	.889	.886	29.72
760	.947	.944	.941	.938	.934	.931	.928	.925	.922	.919	.916	.913	.910	.907	.904	.901	.898	.895	.892	29.92
765	.953	.950	.947	.944	.941	.938	.934	.931	.928	.924	.922	.919	.915	.912	.910	.907	.903	.900	.898	30.12
770	.960	.957	.953	.950	.948	.945	.940	.936	.933	.930	.927	.924	.921	.918	.915	.911	.908	.905	.903	30.31
775	.966	.963	.960	.956	.953	.950	.946	.943	.940	.937	.933	.930	.927	.924	.921	.918	.915	.912	.909	30.51
780	.972	.969	.966	.963	.959	.956	.953	.950	.947	.944	.940	.937	.933	.930	.927	.924	.921	.918	.916	30.71
	59	61	63	65	66	68	70	72	74	75	77	79	81	83	84	86	88	90	92	

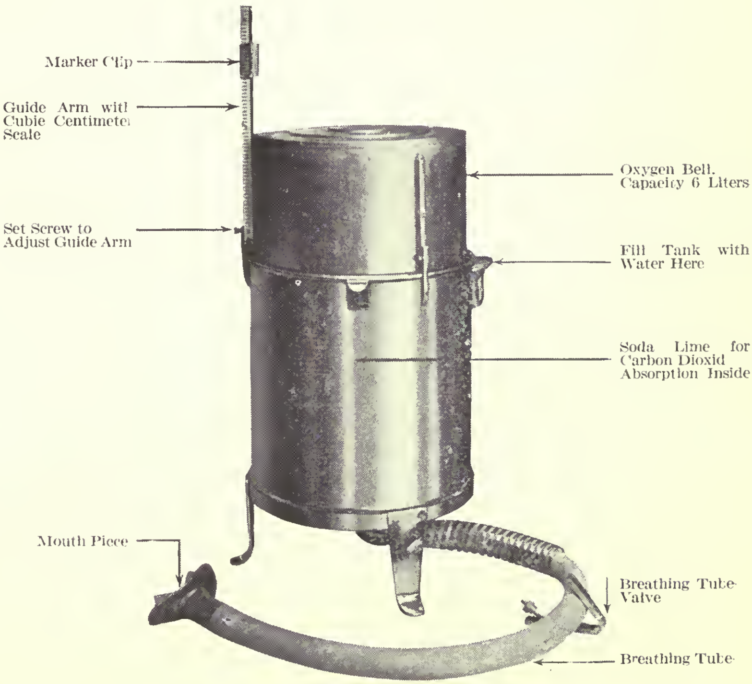
Temperature, Fahrenheit

CHAPTER 12

SANBORN HANDY APPARATUS

By Charles G. Beall M.D.

This apparatus has several advantages. It can be transported in its case any distance and can be easily carried so that a metabolism determination can be made in the home. It does not get out of order as easily nor require as much attention as the larger types of apparatus. While the oxygen bell is not counterbalanced, patients generally take the test better with this apparatus than with our larger one. It may not be quite as



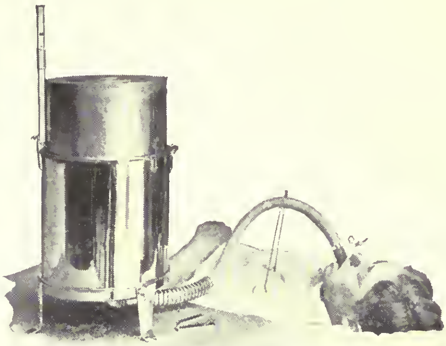
accurate as some of the older types of apparatus, but for clinical purposes it is very satisfactory. The table below gives the comparative readings of oxygen consumption of 10 individuals by the two types of apparatus that I am using.

Normals	*Age*	*Sex*	*Benedict*	*Handy*	*Average*
St. J.	24	M	— 13%	— 2%	— 8 %
C. B.	40	M	— 19	— 14	— 17
E. O.	30	F	+ 9	+ 5	+ 7
J. R.	29	M	— 5	+ 2	— 2
E. B.	19	F	+ 14	+ 15	+ 14
C. M.	27	F	— 0.5	— 7	— 4
Chronic Appendicitis					
M. S.	27	F	— 8	— 3	— 5
Simple Goiter					
P. S.	29	M	+ 98	+ 89	+ 94
Exophthalmic Goiter					
I. R.	23	F	— 18	— 2	— 10
Adenoma of Thyroid					
C. L.	50	F	+ 61	+ 49	+ 55
Exophthalmic Goiter					

The most probable values would be the average. Even with the same apparatus, different readings on the same individual will commonly vary 5 or 10 points in the metabolic rate. Several tests should be made on a patient and the average taken.

Description of Apparatus.—(See illustration). The spirometer bell contains oxygen and moves up and down in a water seal. The patient inhales from and exhales into this supply of oxygen thru a breathing tube entering thru the base of the oxygen chamber. The inhaled and exhaled gases pass thru a container of soda lime inside of the bell, thus removing carbon dioxid from the exhaled gas. The volume of oxygen consumed by the patient is shown by the scale in cubic centimeters. The scale automatically reduces the volume to zero degrees, Centigrade. The mouthpiece, metal connection and breathing tube should be sterilized by boiling before making the determination of the basal metabolic rate.

Testing the Apparatus.— It is of the utmost importance, in testing the metabolic rate of a patient, that there is no leak in the circuit, because the escape of oxygen from the tank, other than that being consumed by the patient, will mean an increase in the final reading, and, consequently, a misguiding result. The question of leakage should be looked after from two different angles, the patient and the machine. A mouthpiece improperly fitted, namely, one which is not overlapped by the lips, is liable to be the source of a leak at the least movement of the patient. Besides, it is very annoying to have a mouthpiece fitted wrongly causing undue discomfort in the mouth, annoying from the



patient's standpoint, because he or she will have to stand it for 10 or 15 minutes, and annoying from the standpoint of the observer because the results will be modified. The nose clip is another factor that may modify the results. It will cause increased oxygen consumption, unless pains are taken to observe that there is no escape of gas. It is customary to fasten the nose clip before adjusting the mouthpiece. When this is done the patient is asked to close the lips tightly and make an expiratory effort through the nose. If there is any leakage the nose clip is tightened and the patient asked to repeat the procedure until we have the certainty that the patient is not allowing the escape of air through the nostrils.

In testing the apparatus itself proceed as follows: Open the breathing tube valve and allow air to enter by lifting the bell to the 4,000 or 5,000 c. c. mark. Close breathing tube valve. Place several small objects on the spirometer bell, not over half a pound, and distributed in such a fashion that the bell remains level. Read the scale again at the end of 10 minutes. Naturally, the second reading should be the same as the first. If it is not, there is a leak in the system. If a leak exists, push the ends of the rubber tubings further on the metal tube thus tightening the connections.

Preparation of Patient.— It is essential that the patient be in the fasting state, i. e., without food for 14 hours. It is best to make the determination in the morning. The usual instructions given the patient are, that he must eat or drink nothing after the evening meal and must not eat any breakfast, nor even drink a glass of water. This is important, as a patient will often take a cup of coffee and say, "that is no breakfast". A difference of 15% has been found in the metabolic rate before and after a cup of coffee. The patient's weight and height, without clothing, are taken, and he or she should then lie down for at least 30 minutes before the test.

Making the Test.— The apparatus is set up. The water seal of the gasometer is filled with water to within 2 inches of the top. The spirometer bell is then filled with oxygen by connecting the breathing tube with the oxygen tank and admitting 4,000 to 5,000 c. c. of oxygen. The breathing tube valve is now clamped tight. At this point it is well to explain to the patient as plainly as possible the object of the test and what is to be done, assuring him that he will have no pain or discomfort and will not be put to sleep, and that the object of the test is to determine how much "pure air" is consumed in 10 minutes. His confidence and co-operation is thus obtained. The nose clip is now adjusted and tested to see that no air escapes thru the nostrils by the procedure above described. The mouthpiece is then handed to the patient, the technician showing him with another mouthpiece just how to introduce it into his mouth. After this is comfortably adjusted he is instructed to exhale and hold the breath until the breathing tube is connected to the mouthpiece and the breathing tube valve released. This takes only a few seconds.

As explained in Chapter 7, care should be used in taking the readings on an apparatus of this sort, to obtain regular breathing. "Irregular expirations, however, deeper or shallower than the average or normal ones, are always more or less numerous, and if the scale is read at the end of one of these considerable error may be introduced." . . . When three or four regular expirations occur, note the height to which the bell rises, and the time. At the end of 5 minutes, again a reading should be taken. Two or three of the 5 minute periods should be run for each test of a patient. If there is a material difference between the 5 minute readings, it is best to repeat the test. (The test sheet shown below is a convenient form to use).

METABOLISM TEST SHEET

Date . . . .

Name . . . . Age . . . .

Height . . . . Weight . . . .

Physician . . . .

Technician . . . .

Time		*Volume*
	. . . . H . . . . M . . . . S . . . . . . c.c.	
. . . . Min.		. . . . c.c.
	. . . . H . . . . M . . . . S . . . . . . c.c.	
	. . . . H . . . . M . . . . S . . . . . . c.c.	
. . . . Min.		. . . . c.c.
	. . . . H . . . . M . . . . S . . . . . . c.c.	

Consumed in . . . . Min. . . . . c.c.

Per Minute . . . . c.c.

Consumption of Oxygen per Minute at 0°C. and 760 mm.

Normal Consumption . . . .

Plus or Minus . . . .

Basal Metabolism in Percentage . . . .

Remarks . . . .

The average amount of oxygen used per minute is now determined. This figure is now corrected for temperature, the temperature being noted on the thermometer inside the oxygen chamber.

With this apparatus corrections for temperature of the gas are easily made. There is a special scale for the volume and "this scale is graduated so that the equivalent volume of gas at 0°C. is read directly from the scale at 19°, 20°, or 21° C." The corrections for volumes read at the temperatures commonly used are as follows:

Degrees Centigrade	*Volume Corrections*
16, 17, 18	Add 1%
19, 20, 21	No correction
22, 23, 24, 25	Subtract 1%

This figure is then corrected for barometric pressure. When the barometer readings are near 760 mm. the corrections may be made by subtracting 1% for each 10 mm. below 760, or adding 1% for each 10 mm. above 760. This now gives the average amount of oxygen consumed per minute at 0° Centigrade and at 760 mm. barometric pressure. Now find what the normal consumption is for this patient's weight and height by referring to the table on page 242 being sure to make the corrections of the figures in the table for age and sex on page 241. The difference between this figure and the actual amount consumed by the patient shows whether the rate is above or below normal. The difference is divided by the normal consumption and the result is the percentage above or below normal or the metabolic rate.

The simplified method of computations that is used with this apparatus reduces the time of computations to less than 5 minutes, and, as I pointed out at the beginning of this article, the results found by use of this apparatus check within clinical requirements.

CHAPTER 13.

VALUE OF BASAL METABOLISM STUDIES[1]

By Albert H. Rowe, M.D.

Metabolism Studies.— All investigators agree that basal metabolism depends largely upon thyroid activity and that an increase in the activity of this gland raises the metabolic rate above normal, while a decrease in thyroid secretion depresses the rate below its normal level. While other ductless glands, especially the pituitary and ovary, control metabolism to a lesser degree, and while certain diseases such as fevers, lymphatic leucemia, hyperpituitarism, polychemia, severe diabetes, cancer and pernicious anemia increase the basal metabolic rate, and starvation, hypopituitarism and wasting diseases decrease it,— all these conditions can easily be ruled out in a careful diagnostic study. Thus, for proper investigation, basal metabolic rate determinations in thyroid disturbances are coming to be recognized as being as indispensable as is the Wasserman reaction in syphilis, or temperature determinations in fever.

Studies made by the Author.— The author has been interested in basal metabolism in thyroid disease since 1915, when he came in intimate contact with the work of Means, Joslin and Du Bois in Boston and New York. This interest was intensified when in the fall of 1920 he watched the work of Boothby and Plummer at the Mayo Clinic, after which he established in his own office a metabolism apparatus. Since then, he has made careful clinical and metabolic studies of some 80 cases of actual and suspected thyroid disturbances and has become convinced of the value of basal metabolic rate determinations as a guide to both the diagnosis and treatment of these conditions.

[1] Editor's abstract of "The Value of Basal Metabolism Studies in the Diagnosis and Treatment of Thyroid Diseases"—Am. Jour. Med. Sc., **162**: 187. August, 1921. Approved by Author.

An Aid to Differential Diagnosis.— Mild or definite cases of hyperthyroidism can be differentiated from neurosis and early tuberculosis by basal metabolic rate determinations. In a series of 49 cases referred to the author, with the diagnosis of actual or suspected hyperthyroidism, only 16, or 39 per cent., had rates above the approximate normal limits of ± 10 per cent. Clinically, all the cases showing rates higher than + 10 per cent. were definitely hyperthyroid. Moreover, with the exception of one, all the other cases that showed normal metabolic rates had one or more symptoms and signs which suggested hyperthyroidism, tho a very careful scrutiny of their records in most cases would incline one to doubt the existence of too much thyroid secretion. It is especially in those cases where a decided exophthalmos is present, where marked tachycardia, nervousness and sweating occurred, or where a tachycardia following a recent tuberculosis persisted. that a method of deciding on the responsibility or harmlessness of the thyroid gland is of great importance. We all see tremulous, nervous, excitable, weak and thin individuals who may or may not be hyperthyroid in type, the definite determination of which state is impossible without such a test as this one we are considering. Clinicians especially interested in heart diseases and in tuberculosis are beginning to see the advantages of these determinations in their diagnostic work. The basal rate determinations are being found of increased value in the analysis of tachycardia.

Test of the Severity of Hyperthyroidism.— Again, the severity of an obvious case of hyperthyroidism can be more accurately determined thru basal metabolic rate determinations than by any other method of analysis. Thus in our series, one case had symptoms which could easily suggest a very severe state of hyperthyroidism, whereas her metabolic study placed her in the mild group of cases. Another case had encephalitis lethargica develop on top of her hypothyroidism, and the problem of how much the thyroid was to blame for the prolonged convalescence and weakness was greatly illuminated by the basal metabolic rate result. Another case which, one year ago, had a marked struma with tachycardia, exaggerated tremor and loss of weight, and who had her septic mouth cleaned up at that time, still presented marked exophthalmos and some tremor. Tho we believed her hyperthyroidism to be considerably diminished, it was a distinct surprise to find a normal rate. In other words, basal metabolism determinations have a definiteness which clinical signs have not.

Guide to Roentgen-Ray Therapy.— As a guide to the amount of roentgen-ray therapy needed in a case of hyperthyroidism due to hyperplasia of the thyroid gland, basal metabolism studies are indispensable and are necessary for scientific work. One of our cases when first seen was a severe type of true hyperthyroidism, and at that time we were not ready to make metabolic rate determinations. Four rounds of roentgen-ray treatment had been given when her first test was made, and in view of her increased weight, slower pulse, great improvement in her nervous condition and her increased strength, together with a rate of only + 7 per cent., we discontinued roentgen-ray therapy for one month. By that time her clinical condition was not quite so favorable and her rate had risen to + 12 per cent., because of which another round of roentgen-ray was given. . . . Another case, with a rate of + 10 per cent. after 11 roentgen-ray exposures, had marked hyperthyroidism before treatment. . . . Another has had definite amelioration of symptoms and reduction in rate by the use of roentgen-ray over several months. . . . Our experience, therefore, indicates a definite beneficial effect of roentgen-ray treatment in cases of true exophthalmic goiter.

The amount of therapy necessary to reduce the metabolic rate to normal limits certainly varies with the case. That there is danger of too much roentgen-ray is certain. Moreover, roentgen-ray will probably be found ineffective in fulminating cases. . . . With the increasingly low mortality after operative treatment in mind, we cannot at this time recommend roentgen-ray as a substitute for surgery in all cases of hyperthyroidism. However, when it is used the effect must be carefully followed by metabolic rate determinations. This is especially emphasized by an experience of a colleague in another city whose patient remained well for two years after a thyroidectomy. He then became weak and nervous, and as his condition suggested a return of the hyperthyroidism, he was sent for roentgen-ray therapy. Soon afterward a metabolism test disclosed that he had a —35 per cent. rate and, upon the administration of thyroid gland, his condition immediately improved. Here roentgen-ray was being administered where it was absolutely contraindicated and the error was discovered only thru metabolic rate studies. All doubtful cases of mild hyperthyroidism should have their rates determined before roentgen-ray therapy since many innocent thyroids are roentgen-rayed when they should be left entirely alone.

An Index to Toxicity of Adenomas of the Thyroid.— Another use of the metabolic rate lies in the indication given as to the degree of toxicity of adenomas of the thyroid. It is well known that adenomatous thyroids may produce no symptoms of hyperthryoidism or that all symptoms of Graves' disease may occur. Thus the finding of rapid pulse, nervousness and tremor in the individual with an adenoma of the thyroid calls for a determination as to the responsibility of symptoms; whether the gland has taken on excessive secretory activity or whether a neurosis or sympathetic stimulation is causative. . . . One of our cases, with a metabolic rate of + 53 per cent. after very extensive roentgen-ray therapy, illustrates the opinion of roentgenologists today that hyperthyroidism due to adenomatous thyroids is not benefited by roentgen-ray treatment in the marked degree that hyperthyroidism due to hyperplasia of the gland is by such treatment. This woman, subjectively, feels a little better but her thyroid is still very active, as shown by her symptoms, and especially by her recent rate of + 57 per cent. Another case had been diagnosticated as having a toxic adenoma, and before metabolism determinations had received 3 rounds of roentgen-ray with no amelioration of symptoms. The normal rate recently obtained probably indicates that the symptoms for which she was being treated by roentgen-ray were neurotic in nature. Still another case had an intrathoracic adenoma and recently had been told that she was extremely toxic, as indicated by a marked tremor and subjective nervousness. Here again the rate was found to be normal, indicating a functional rather than a toxic nervousness.

A Guide to Surgery.— As a guide for the surgical removal of hyperplastic, colloid and adenomatous thyroids, metabolic rate studies have gained recognition from the leading goiter men of the country. Means emphasizes the importance of these tests before surgery and, with Boothby, feels that when rates of over + 70 per cent. are found, rest or ligation should be resorted to before thyroid removal. . . . It is generally conceded by surgeons, however, that the metabolic rate is not an inflexible guide, and that even when the rate is high, if the clinical condition be favorable, it is probably safe to operate. . . . As before stated, adenomatous thyroids must be treated surgically, since the metabolic rates are not easily reduced by roentgen-ray.

A Method for Diagnosis of Hypothyroidism.— In diagnosing hypothyroidism and myxedema, metabolism tests hold as important a position as in the diagnosis of hyperthyroid states. Clinicians are always presuming lack of thyroid secretion because of dry skin, thin hair, slow pulse and obesity. Analysis of such cases very often shows a perfectly normal rate and indicates that the responsibility of the symptoms can not be attributed to thyroid activity. Thus in 25 cases recently referred, with the possibility of hypothyroidism, only 10, or 40 per cent., had metabolic rates sufficiently low to indicate too little thyroid, or the possibility of other ductless gland inactivity. Of these 25 cases, 10 were extremely obese and could easily suggest the lack of thyroid secretion; none of these, however, showed rates below normal limits. . . . One of the cases referred, when first seen a year ago, was a typical advanced case of myxedema with anemia, non-pitting edema and mental disturbances. At present she is taking thyroid very intermittently and feels well, altho her rate is still —28 per cent.

A Guide to Thyroid Therapy.— Finally, as a guide to correct thyroid administration, metabolic rate determinations are of the greatest value. As already stated, hypothyroidism with consequent thyroid therapy is undoubtedly often misdiagnosed. Metabolic studies, moreover, as pointed out by Means, usually show that it takes much less thyroid to keep that rate at normal than is usually administered; furthermore, it is found that the rate can be elevated considerably above normal without clinical symptoms of hyperthyroidism being evident. That such therapy does harm, even tho these symptoms are not present, is shown by a case recently seen in which thyroid administration in rather large dosage for obesity suddenly produced a dilated thyrotoxic heart. This emphasizes the necessity for the use of the metabolic rate studies as a means first, of being sure of your clinical diagnosis, and second, of gaging the amount of thyroid therapy. At present, in the use of the dry thyroid gland, we have little idea of the strength of the preparation. Kendall has shown that the amount of thyroxin in thyroids varies according to seasons. . . . Plummer has shown that 1 mg. of this thyroxin raises the metabolic rate about 2 per cent. and that it takes about 1 mg. per day to keep the rate of a myxedematous patient up to the normal. However, he determines his dosage by metabolic rate studies. . . . We feel that thyroid administration to children should be guided, if possible, by metabolic studies, and that these studies should be the basis for the diagnosis of mild hypothyroid states that are so often assumed by clinicians in their young patients. No child should receive thyroid simply because he looks "a little hypothyroid in type."

Conclusions.— The importance of basal metabolism studies in the handling of thyroid diseases must be recognized. By metabolic rate determinations we are greatly aided in our diagnosis of early and obscure cases of hyperthyroidism. Moreover, the degree of severity of an obvious hyperthyroidism can be determined by this test. Again the presence or absence of toxicity of an adenomatous thyroid is made evident thru these metabolic studies. As a guide for surgical removal of goiters, surgeons are recognizing the value of this test. Finally, in the diagnosis of hypothyroidism and in directing and gauging thyroid administration, metabolic rate determinations are of the greatest importance.

CHAPTER 14.

BASAL METABOLISM AND THE GENERAL PRACTITIONER[1]

By James H. Hutton, M. D.

Variations in Thyroid Activity.— In automobile language the thyroid is the ignition system of the body. Under certain conditions any increase or decrease in heat production is usually due to a corresponding change in thyroid activity. The two extremes of its activity are easily recognized. The picture of well-marked Graves' disease, and of the cretin, are almost as familiar to the laity as they are to the profession. It is the borderline case, where either a slight hypothyroidism or a slight hyperthyroidism exists that is hard to recognize.

Up to date the best measure of the degree of thyroid activity is the determination of the basal metabolic rate. Certain conditions cause variations from the normal limits, hyperthyroidism probably being the most frequent cause of an increased rate. Febrile conditions, leucemia with large numbers of white cells, and acromegaly are also causes of an increased rate. Hypothyroidism is the most frequent cause of a decrease in rate.

Carbohydrate tolerance, which is another gross measure of metabolism, is usually decreased in the hyperthyroidic and increased in the hypothyroidic condition of the gland. Men who are doing a large amount of work with these tests feel that the determination of the basal metabolic rate is a much more accurate measure of the activity of the thyroid than any other test in use at this time.

As a Differential Diagnostic Measure.— Incipient tuberculosis is hard to differentiate from hyperthyroidism. Many cases are sent to sanatoria every year, only to be sent home when their rate is found to be 15 to 20 per cent. above normal. So far as

[1] Editor's abstract of "Basal Metabolism and the General Practitioner", Ill. Med. Jour., June, 1921. Approved by author.

known, tuberculosis does not cause an increase. Organic heart disease, incipient tuberculosis and hyperthyroidism many times resemble each other very closely. A knowledge of the basal metabolic rate will enable one to decide with a great deal of certainty whether the thyroid is at fault.

Case Reports.— Clinically it is often difficult to distinguish hyperthyroidism from hypothyroidism. As an example: Last winter Mr. W. had the flu. His recovery was slow and after a time he developed tachycardia, a tremor, loss of weight and other symptoms of hyperthyroidism. A number of physicians saw him and all were more or less agreed that his illness had precipitated an attack of hyperthyroidism. A surgeon advised operation as soon as the patient could stand it. Soon after this his basal metabolic rate was found to be 20 per cent. below normal. He recovered when given thyroid gr.i.t.i.d.

Recently Janney and Henderson have called attention to "latent hypothyroidism." Most of us probably have such cases under observation. For instance, Mrs. G., 30 years of age, complained of various pains in her back, arms and hands. She had little "pep", but little appetite and no ambition; wanted more sleep than the average person and indulged in bad dreams while getting it. Her family and past history seemed to have no bearing on her present trouble. She had a negative Wasserman and negative physical examination. She had a slight degree of anemia. Her blood pressure was 110-70-40 and her urine was low in specific gravity and urea. Her basal metabolism was 12 per cent. below normal. Her friend, who referred her to me, said that the patient's only trouble was that of many American women — too much money and time, too little responsibility, and a too active imagination — and yet under the influence of thyroid combined with a little ovarian substance and small doses of pituitary, she soon became able to take an interest in many things besides her own aches and pains.

Value of Basal Metabolism Determinations.—The determination of the basal metabolic rate in such cases may mean that many so-called neurasthenics can be changed from bores, for whom nothing can be done, to interesting cases for whom a great deal can be accomplished. This test for basal metabolism is a measure almost strictly diagnostic, and gives us exact and valuable information where formerly we had none. It in no way relieves us of the responsibility of taking case histories and making the usual physical examination and laboratory tests. In fact, the finding of a basal metabolic rate outside the normal limits should, in many cases, stimulate us to make a more careful examination and a more detailed inquiry into the patient's history—especially the family history and the developmental period of the patient's life.

The General Practitioner's Opportunity.—To us, as general practitioners, a knowledge of basal metabolism is of especial value. We see these cases early and if we can make a diagnosis promptly and institute proper treatment, they may never reach the stage where the specialist is called. If the specialist is called, and we have made the diagnosis, no one can complain that the patient's life might have been saved if only Dr. So-and-So had been alive to the situation. We probably overlook the hypothyroidic condition more often than the hyperthyroidic; yet the former is the condition offering the greatest opportunity for brilliant cure.

CHAPTER 15.

BASAL METABOLISM IN VARIOUS DISEASES

By H. O. Mosenthal, M. D.

Facts of importance to clinical medicine have been obtained by the study of basal metabolism in obesity, cardiorenal disease, nephritis, pernicious anemia, leucemia, and diseases of the thyroid gland. The following table, taken largely from the writings of Du Bois and his collaborators (altho other sources have been consulted) indicates the variation in basal metabolism that has been observed in these diseases:

BASAL METABOLISM AS REPORTED IN VARIOUS DISEASES

	Per cent. basal metabolism above or below average normal
Normal	—15 to +15
Obesity	—14 to +10
Cardiorenal without dyspnea	—10 to +10
Cardiorenal with dyspnea	+25 to +50
Nephritis with edema	—40 to +14
Nephritis without edema	+ 2 to +29
Pernicious Anemia	+ 2 to +33
Leucemia	+21 to +123
Prolonged undernutrition	—30 to —10
Exophthalmic Goiter:	
Very mild	+15 to +30
Mild	+30 to +50
Severe	+50 to +75
Very severe	Over +75
Cretinism and Myxedema	—40 to —15

[1] Editor's abstract of "The Clinical Value of Basal Metabolism. The Determination of Basal Metabolism by Means of the Benedict Portable Respiration Apparatus. Facts of Importance to Clinical Medicine that have been obtained by the Study of Basal Metabolism in Obesity, Diabetes Mellitus, Cardiorenal Disease, Nephritis, Pernicious Anemia, Leucemia, Typhoid Fever, and Diseases of the Thyroid Gland." Medical Clinics of No. Am. March 1921, 4: 103. Approved by Author.

Obesity.— There are some cases of obesity which are due to disturbances of the internal secretions. The types brought on by the diminished activity of the thyroid and hypophysis are familiar to all, and may be diagnosed in large part by their clinical characteristics. In doubtful cases, however, a determination of the basal metabolism will be of very great help. In the hypothyroid cases the basal metabolic rate is below normal. In the more common form of obesity, due to overeating, physical inactivity, and a placid disposition, the metabolism, as measured by the surface area, is within normal limits. Evidently the increased body bulk, due to the "inert fat", has not the same effect in reducing metabolism as the "inert fluid" has in edematous patients. The former are up and about and the latter are usually bedridden and undernourished; these differences may be the determining factors in maintaining or lowering the basal metabolism. In treating obesity it is obvious, in view of the normal metabolic rate that exists in these individuals, that the addition of thyroid preparations to the subcaloric diet as an "accelerator" for the loss of weight, must be carefully watched. In these cases, symptoms of hyperthyroidism often follow even comparatively small doses; tachycardia, cardiac irregularities, headache, nervousness, restlessness, diarrhea are prone to develop and must be guarded against. In every case of obesity loss of weight does not ensue upon the use of thyroid medication, tho the drug is given to the point of mild intoxication.

Nephritis and Heart Disease.— In cases of mild nephritis and compensated cardiac disease the basal metabolism ranges within normal limits. In some instances in cardiorenal patients the metabolism rises as high as 50 per cent. above the average. Dyspnea is the factor that produces this change; the muscular effort entailed by the increased respiratory rate is presumably responsible. On the other hand, in some cases the basal metabolism is considerably lowered; in patients who have much edema it may be as much as 40 per cent. less than the average. The edema increases the surface area by distention with an inert fluid, and it is probable that a lower metabolism as measured by the surface area should be present under such circumstances. A rise in blood pressure, the presence of an acidosis or even the existence of marked impairment of renal function, as measured by the conventional tests, does not influence the plane at which metabolism proceeds. The abnormally high metabolism occurring in certain nephritics has been attributed to the dyspnea and restlessness characteristic of the severe types of the malady; previous fasting and undernutrition may be responsible for some of the low figures presented. Furthermore, a study of the respiratory quotients makes it evident that the metabolism of proteins, fats, and carbohydrates is not disturbed in the cases of heart and kidney disease thus far observed in the calorimeter.

In isolated instances in very severe nephritis a determination of the nitrogen balance has shown that a toxic destruction of protein must exist at times at least. This apparently occurs most frequently when such patients are moribund and the phenomenon thus assumes a position of minor clinical importance.

From the physician's point of view some of these facts are of very great value. Dyspnea and edema in themselves demand immediate symptomatic treatment, and the determinations of basal metabolism are not of any aid in making either the diagnosis or therapy more precise. The knowledge that hypertension, acidosis, and renal insufficiency do not alter the metabolic rate or result in any change in the nephritic or cardiac patient that impairs his ability to utilize proteins, fats, or carbohydrates, gives the clinician a very sound foundation upon which to proceed when the very important dietetic side of the treatment is determined upon in this group of cases.

Pernicious Anemia. — The increase of basal metabolism present in pernicious anemia may be somewhat unexpected. The languor of such patients certainly does not indicate it. The rapid regeneration of blood-cells, and the extra effort required from weakened and impaired muscles in carrying out the bodily functions, especially the respiration and circulation, with the increased frequency of the respiratory rate and the heart-beat, may explain the rather marked rise in basal metabolism occurring in anemia. These observations indicate why rest and a high caloric regime are efficacious in bringing about an amelioration of the condition. The high diet is generally acknowledged as being desirable, but it is carried out conscientiously in but few cases. This is partly due to the fact that many of these patients have poor appetites, and, in part, it may be attributed to the lack of care in administering such diets. It is a common experience that "forced feeding", when it is actually analyzed, really provides a subcaloric ration. In those cases in which a high diet of 3000 to 5000 calories has been carried out the results have been remarkably good; the red blood-cells have increased and the general condition has been improved.

Leucemia. — The very high basal metabolism characteristic of leucemia is extremely interesting. The rise is so great that the only theoretic explanation of this state of affairs does not seem to be entirely adequate; it is claimed that the process producing the great number of white blood-cells may be responsible for the increased metabolism; whether other factors also play a rôle remains to be determined. It is perfectly evident from the facts thus far obtained that these cases must have a diet of a caloric value considerably in excess of the normal if they are not to become weak and anemic.

Further, from the above table it may be noted that cardiac disease, undernutrition, obesity, and certain nervous affections may lead to the suspicion that the thyroid gland is functioning too actively or too little. In the event of necessity of differential diagnosis under these circumstances, the determination of the basal metabolism is of very great help, inasmuch as all of the conditions mentioned vary much less from the average normal basal metabolism than do abnormal thyroid states.

CHAPTER 16

THE BASAL METABOLIC RATE IN ENDOCRINE DISTURBANCES[1]

By John L. Tierney, M. D.

The value of the basal metabolic rate in the determination of the activity of other glands than the thyroid, for example, the pituitary and gonads, is less clear, and to venture in a small way to throw more light upon this phase has been the purpose of this paper, in the construction of which writer has studied:

40 Cases Hyperthyroidism
49 Cases Hypothyroidism
22 Cases Hypopituitarism
4 Cases Hyperpituitarism
6 Cases Diabetes Insipidus
22 Polyglandular Cases, involving disturbances of the Pituitary, Gonad and Thyroid Glands.

Dualistic Function of the Hypophysis.— From fundamental, experimental, and clinical knowledge of the hypophysis, it is quite definite that this gland exerts a control upon metabolism, and it is logical to assume that in disturbances of the hypophyseal function the basal metabolic rate should be modified, and, if this be true, should be an index to the physiological activity of the gland. A wealth of pathological, clinical, and experimental fact supports certain considerations concerning the hypophysis — *i. e.*, that the anterior lobe regulates and controls:

1. The skeletal, cuticular and subcuticular growth;
2. The function and development of the gonads and the secondary sexual characters;

and that the posterior lobe is concerned with:

[1] Editor's abstract, "The Basal Metabolic Rate in Endocrine Disturbances," Med. Clinics No. Am., 4:775, Nov. 1920. Approved by author.

1. The regulation of carbohydrate metabolism, glycosuria, hyper-glycemia and obesity;
2. The contraction of the involuntary muscles, peristalsis, uterine contraction, etc., and
3. The renal secretion, polyuria, blood pressure and body temperature.

Notwithstanding these facts there has been considerable argument concerning the functions of the hypophysis cerebri and its effects upon metabolism, particularly carbohydrate tolerance and the basal metabolic rate. Means found a decreased basal metabolic rate in hypopituitarism with obesity; and Magnus-Levy an increased rate in acromegaly. Cushing maintains that when the posterior lobe is rendered inactive by disease or compression, metabolism procedures are checked and a high tolerance is acquired for carbohydrates, which are promptly stored as *fat*. Robertson states that pathological conditions partially or totally destroying the function of the anterior lobe produce the clinical picture of *adiposity*, under-development of skin, bone, primary and secondary sexual characteristics, etc. Snell, Ford and Rowntree state — "Hyperactivity of the anterior lobe occurring in youth results in gigantism, and in adults, in acromegaly; functional hypoactivity results in infantilism."

A marshalling of the available facts regarding the physiologic action of the pituitary gland reveals that the function of the gland is dualistic. The component parts are embryologically, histologically, and physiologically distinct. These physiologic differences are manifest thru the hormonic signs, both subjective and objective, such as amenorrhea, dysmenorrhea, epileptiform attacks, somnolence, obesity, headaches, different changes in the osseous, genital and dermal symptoms, blood pressure, temperature, involuntary muscle contraction, etc.

Diagnosis of True Hyposecretion.— In studying the cases on record we note that certain cases may show physical evidence of hyperfunction and physiologic evidence of hypofunction. For instance, an acromegalic (or post-adolescent anterior lobe hypersecretion) may change into hypo-secretion, retaining the gross physical characteristics of acromegaly but exhibiting the functional features of hypoactivity, such as myasthenia, decreasing mentality, loss of libido, etc. In this type of case the determination of the basal metabolic rate we believe is particularly valuable because it serves as an index to the physiologic state at the time of observation, and to the proper procedure in a therapeutic way.

Pluriglandular Syndromes.— Such combinations as thyroid and pituitary deficiency are exceedingly common. In our classification this diagnosis has been based upon the associated hormonic signs, and from the prominence of certain hormonic signs we believe it has been possible to distinguish the particular gland in which deficiency is most marked. The thyroid and pituitary insufficiency have showed most striking decreases in basal metabolism, but we have some cases showing absolutely no hormonic evidence of thyroid deficiency which have been classed as pituitary and gonadeal insufficiency showing very definite decreases in the basal metabolic rate.

Gonadeal Deficiency.— In connection with deficiency of the gonads, we recognize certain gross metabolic effects such as changes in skeletal growth, development of dermal appendages and characteristic obesity. Whether these effects are primarily gonadeal or the results of secondary, reciprocal endocrine effects is a question. The writer has seen a decreased metabolic rate in a number of cases that have been deemed pure gonadeal insufficiencies and showing no clinical evidence of reciprocal thyroid or pituitary involvement. It must be admitted, however, that most testicular and ovarian insufficiencies have been definitely associated in a clinical way with other glandular insufficiency, to such an extent that it is difficult and ill-timed to attribute a decreased basal metabolism to a primary gonadeal deficiency.

Conclusions.— In the case of polyglandular insufficiency, the basal metabolic rate has been consistently decreased. The most notable decreases have occurred in cases in which there was an associated hypothyroidism. We have come to the conclusion that the determinations of the basal metabolic rate are valuable in the study of endocrine disturbances, and that determinations of carbohydrate tolerance are of *definitely lesser value.* Despite the fact that the method is being severely criticized, and even discarded by some observers, we feel that the determinations of the basal metabolic rate are destined to become an integral part of diagnostic procedure, not only in the measurement of thyroid activity but in the determination of pluriglandular, pituitary and possibly gonadeal and adrenal activity as well. It must be remembered that the physical characteristics and signs give evidence of certain endocrine states, but it must also be recalled, as Marie long ago pointed out, that hyperactivity can be transformed into a state of hypoactivity retaining the physical characteristics of hyperactivity but possessing the physiologic functions of hypoactivity. The basal metabolic rate will help us, we believe, to determine the physiologic activities of certain glands at the time of observation, independently of what their previous activities may have been. This determination of the physiologic activities at the time of observation is of paramount importance because it is, we believe, the most logical index to diagnosis, prognosis, and, what is of greater importance, proper therapy.

CHAPTER 17

DYSTHYROIDISM

By J. Earl Else, M. D.

A careful study of the clinical manifestations of hyperthyroidism in conjunction with the basal metabolic rate shows that there is quite a group of cases in which the two do not coincide. Some patients with symptoms of mild hyperthyroidism have normal basal metabolic rates, while other patients who do not appear to have hyperthyroidism show increased metabolic rates. To this group of cases, Janney has applied the term "dysthyroidism".

Outline of Chapter.— This chapter is not intended to be an exhaustive study of dysthyroidism, but is, instead, a brief statement of the conclusions arrived at from a study of a group of cases, and is written with the hope that it may throw some light upon the problem. The cases were classified as follows:

I. Basal metabolic rate lower than the symptoms would indicate.

1. Non-thyroid lesions.
   - A. Chronic tonsil infection.
   - B. Incipient tuberculosis.
   - C. Asthenia with ptosis.
   - D. Double oophorectomy.
2. Hyperthyroidism in the stage of remission.
3. Recurrent attacks of hyperthyroidism.
4. Permanent lesions after recovery from hyperthyroidism.
   - A. Patients normal except for persistent symptoms.
   - B. Mixed symptoms of hyper-and hypothyroidism.

II. Basal metabolic rate higher than symptoms indicate.

1. Early cases of severe hyperthyroidism.

Non-Thyroid Lesions.— The symptoms of other mild toxemias do not differ materially from the symptoms of mild hyperthyroidism. The patients studied had goiters varying in size, which were either colloid or adolescent in type. In general, the patients complained of tiring easily, tachycardia, and palpitation of the heart. Many were irritable, and complained of being "nervous". The majority of them were undernourished, although some were well nourished. The pulse rate varied from 80 to 120 in different cases. Tremor of varying degree was present in a considerable number, and in some the eyes were prominent, although the other signs found in exopthalmos were absent. (A) The majority of the cases were due to chronic tonsil infection, and the removal of the tonsils was followed by a satisfactory recovery, proving the diagnosis. In no case was the removal of the tonsils followed by a reduction in the size of the thyroid gland. However, this does occur sometimes, but it is, I believe, usually a coincident rather than a direct result, for it is very doubtful if there is any relationship between infected tonsils and goiter. In the Pacific Northwest, goiter is very frequent, as are also infected tonsils, so that of necessity the two lesions must frequently appear in the same patient. The tonsil infection appears to be about equal in the two sexes, while goiter occurs much more frequently in the female. If there were any direct relationship between the tonsil infection and the goiter, then the goiter would be expected as frequently in tonsil cases in the male as in the female,which is not the case. Adolescent goiter is much more frequent in the female than in the male.

(B) Incipient Tuberculosis. Very early cases of tuberculosis often give a history and findings similar to early hyperthyroidism, with the exception that the basal metabolic rate is within normal limits. Later, as pointed out by McBrayer, the basal metabolic rate may rise, but it is always low as compared with the symptoms.

(C) Asthenia with Ptosis. Asthenia with ptosis when combined with a small goiter is apt to be regarded as a case of hyperthyroidism. The patients often complain of nervousness, being irritable, rapid heart, loss of strength and weight. Physical findings may show a rapid heart, and some tremor, so that the picture will be suggestive of mild hyperthyroidism. The basal metabolic rate, however, will be within the normal limits.

(D) Double Oophorectomy. The author has seen one patient who had had a dread of goiter since childhood. She gave a history of having had a double oophorectomy at the age of thirty. Following that there was some enlargement of the thyroid gland. This patient came complaining of a goiter, rapid heart, and "nervousness". Examination showed her to be fairly well nourished, pulse 96, coarse tremor, exaggerated reflexes, and a small goiter. Her palms were dry. The basal metabolic rate was between the average and the lower normal limit.

Hyperthyroidism in the Stage of Remission.— Exophthalmic or hyperplastic goiter runs a more or less definite course that can be divided into four stages: first, the stage of development, in which the basal metabolic rate runs higher than the symptoms would indicate; second, the stage of maximum intensity, in which the basal metabolic rate runs about parallel with the symptoms, third, the stage of retrogression, in which the basal metabolic rate falls more rapidly than the improvement of the symptoms would indicate; fourth, the stage of remission, in which the basal metabolic rate is around the normal although the symptoms of hyperthyroidism are still present. Some cases recover, but the majority have recurrences.

During the stage of remission, the symptoms that were present in the attack will often persist. Thus, the patient will come complaining of tachycardia, nervousness, and tiring easily. In some of them, often upon exertion or excitement, the heart will become quite rapid. Examination shows a moderately enlarged heart, a tremor varying in degree, exophthalmos if exophthalmos was present in the attack. On determining the basal metabolic rate, it is found to be within the normal limits. The past history is of great importance in making a diagnosis. If the patients are kept under observation over a long period of time, exacerbations in which there is some rise of the basal metabolic rate will be observed.

Recurrent Attacks of Hyperthyroidism.— Sometimes these patients appear to be quite sick, and yet the basal metabolic rate shows only a moderate increase. This can probably be best explained as follows: The administration of thyroxin over a long period of time or the rapid administration over a short period of time produces persistent lesions and a hypersusceptibility to thyroxin. An attack of hyperthyroidism lowers the resistance of the patient, so that exertion, fright, or worry often shows quite marked exacerbations, although the activity of the thyroid gland as measured by the basal metabolic rate is but little increased.

Permanent Lesions Following Recovery From Hyperthyroidism.— Two groups of patients belonging to this type were seen: first, (A) those in which the patients were normal except for symptoms of hyperthyroidism. When thyroxin is administered over a long period of time or in large amounts, permanent lesions are produced in the heart muscle, central nervous system, behind the eyeball, and elsewhere. Although these patients may completely recover so far as the secretion of the thyroid gland, as indicated by the basal metabolic rate, is concerned, the heart may remain a damaged heart, with tachycardia and irregularity present. The tremor may persist, the patient may still be irritable, and a certain amount of exophthalmos remain because irreparable damage due to the excess of thyroxin.

In the second group of patients, (B) there was a deficiency in thyroid secretion, so that the patient showed the evidence of hypothyroidism in addition to the persistent symptoms of hyperthyroidism. In mild cases, the hypothyroidism may be manifest only by a lower metabolic rate, but in the more severe cases the symptoms of hypothyroidism are present in varying degree.

Early cases of Severe Hyperthyroidism.— In the beginning cases of hyperthyroidism, the basal metabolic rate appears in advance of the symptoms. It rises more rapidly than the symptoms develop. In severe cases, the rate may become very high before clinical manifestations become pronounced.

A study of the group of a typical cases such as that upon which this chapter is based confirms the findings of those who have studied typical cases. The basal metabolic rate is the most accurate index of thyroid activity, but important as the basal metabolic rate is, the history and clinical picture can not be neglected. The symptoms in hyperthyroidism, as in other toxemias, vary with the susceptibility of the patient to the toxin as well as with the amount of toxin. In the more susceptible patients, especially those having a recurrence after previous severe attacks, the patient may be in a precarious condition and have only a low rate, and in the stage of remission, the rate may be normal and yet there may be marked evidence of the recent attack present. Thyroid therapy should always be controlled by basal metabolic examinations.

CHAPTER 18

INTERPRETATION OF BASAL METABOLISM IN HYPERTHYROIDISM

By J. Earl Else, M. D.

The influence of the thyroid gland upon the basal metabolic rate has been fairly well established, but its value to the clinician depends upon its interpretation. The estimation of the basal metabolic rate to the trained observer is not hard, but its interpretation is sometimes quite difficult, and to be made only in conjunction with a thoro knowledge of the patient's physical condition.

Definition of Hyperthyroidism.— Hyperthyroidism is a clinical term used to include those diseases of the thyroid gland in which there is an excessive secretion of thyroxin. It does not include non-toxic lesions. Some lesions, as the adenomata, may be non-toxic at first and later become toxic. As the term is a clinical one, these lesions can not be properly classified in the hyperthyroid group until hypersecretion begins, for many patients have adenomas without ever becoming toxic.

Classification of Hyperthyroidism.— In order to properly interpret the basal metabolic rate in hyperthyroidism, the pathology must be understood. Hyperthyroidism may be either functional or organic. Organic hyperthyroidism may be due either to hyperplasia and hypertrophy, or neoplastic growths, usually benign, but sometimes malignant. Excluding the functional hyperthyroidism and the hyperthyroidism from malignancy, toxic goiter may be divided into 2 types: first, exophthalmic or hyperplastic goiter; and second, cardiovascular goiter.

Exophthalmic or Hyperplastic Goiter.— This is a distinct clinical and pathologic entity running a more or less definite course, during which there is a fairly definite relationship between the pathologic and clinical manifestations. The pathologic course may be divided into 4 stages. First, the stage of development. Microscopic examination shows that there is a diffuse hyperplasia and hypertrophy of the parenchyma. The acini are lined with tall columnar epithelium, contain but little or no

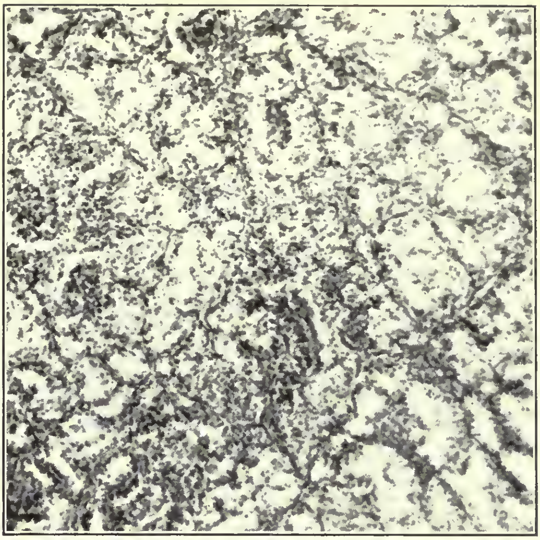


Fig. 1. Exophthalmic or Hyperplastic Goiter. Stage of Development.

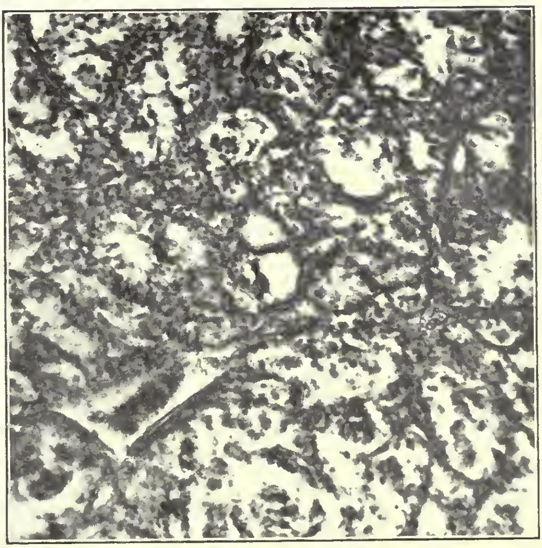


Fig. 2. Exophthalmic or Hyperplastic Goiter. Stage of Maximum Intensity (early)

colloid, and have projecting into them papillomatous-like masses. The absence of colloid in the acini is not to be taken as an indication that the thyroid gland is not secreting. Colloid is not absorbed readily, its purpose apparently being to hold thyroxin and regulate its absorption. In hyperplastic goiter, the thyroxin is not only secreted more rapidly than normal, but on account of the absence of colloid secretion, it is absorbed as rapidly as it is secreted (Fig. 1). Second, the stage of maximum intensity. As the hyperplasia increases, the acini may become completely filled with papillomatous-like masses. In the latter part of this stage, secretion begins to accumulate in the acini, distending them more or less. This secretion begins to take the eosin stain, indicating that colloid is again being secreted (Fig. 2). Third, stage of retrogression. The acini are distended with a deeper staining secretion and contain desquamated cells singly or in masses. The epithelial cells lining the acini approach the normal in size and arrangement, altho hyperplasia and hypertrophy are still present (Fig. 3). Fourth, stage of remission. Although the pathology in the first 3 stages is fairly constant, in the fourth stage there is considerable difference in the different cases. In some there is much hyperplasia and hypertrophy, and papillomatous masses are present. In others the acini appear quite normal, but here and there, rudimentary papillomata are seen. The microscopic picture may present a mixt appearance. In places there may be quite thick masses of connective tissue. Clinically, with the exception of the stage of remission, the symptoms correspond quite closely with the pathologic process, both as to course and intensity. Plummer has listed the symptoms in their usual order of occurrence as follows: Cerebral stimulation, vasomotor disturbance of the skin, tremor, mental irritability, tachycardia, loss of strength, cardiac insufficiency, exophthalmos, diarrhoea, vomiting, mental depression. In the stage of remission there are persistent symptoms, the intensity of which varies with the intensity and frequency of the attacks.

Basal Metabolic Rate and Clinical Manifestations.— Hyperplastic goiter shows an increase in the basal metabolic rate before the appearance of symptoms. The length of time elapsing between the beginning of an increase in the rate and the approach of other clinical manifestations varies with the severity of the disease. In many cases formerly included under effort syn-

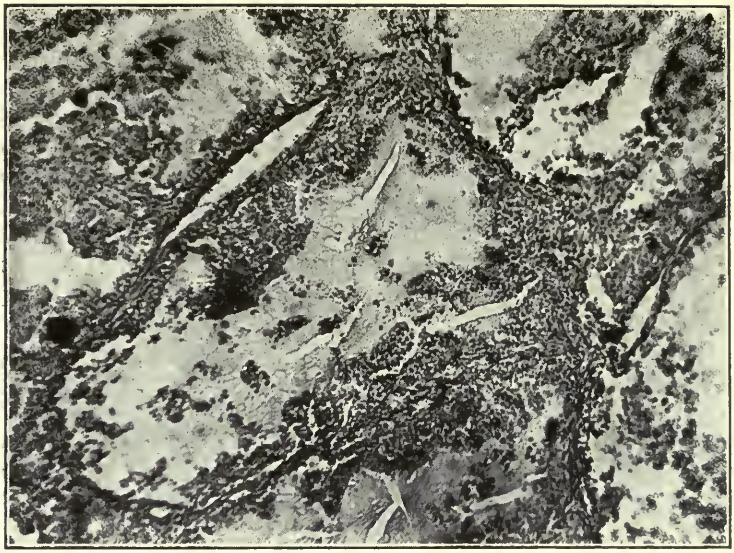


Fig. 3. Exophthalmic or Hyperplastic Goiter. Stage of Retrogression.

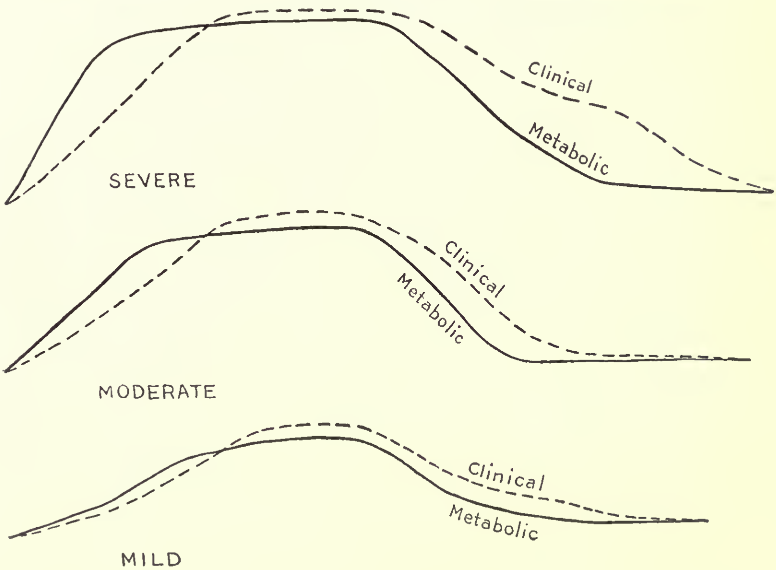


Fig. 4. Schematic Illustration of the Relationship, in cases of Hyperthyroidism, of the Basal Metabolic Rate to the Clinical Manifestations.

drome, but now recognized as early cases of hyperthyroidism, the condition improves, and the patient recovers without showing the symptoms generally looked upon as those of toxic goiter. As a rule, the usual clinical symptoms appear shortly after the basal metabolic rate appears, and rise with the rate (Fig. 4). When the disease reaches its height, both remain stationary, and then start downward. In mild cases, the symptoms follow the rise and fall of the rate quite closely, but in severe cases, the symptoms do not develop as rapidly as the rate increases, and fall much more slowly in the third stage than does the rate. In the very severe cases, the symptoms may follow rather slowly. In the mild cases, the rate may return at once to normal, and remain there, but in the majority of cases, it fluctuates for a time at least. The lower limit may be below normal, while the upper limit varies with the intensity of the recurrence or recrudescence. Patients with a fluctuating rate are rarely clinically normal. In some cases, the patients completely recover, and the rate and symptoms become normal, but many cases pass into the stage of remission which is followed by recrudescence. In the stage of remission, the rate is around the normal, often being slightly subnormal. In one case studied that was in the stage of remission, considerable damage had been done to the heart, so that while the patient was under observation previous to operation, she had cardiac manifestations following exertion or excitement, although the basal metabolic rate was persistently between the average and the lower normal limit.

In general, it may be said that the rise of the basal metabolic rate is the first evidence of hyperthyroidism regardless of the type of lesion producing it. As the disease increases in intensity, the rise of the basal metabolic rate leads the clinical manifestations. The more severe the onset, and the more severe the course, the higher the rate will be in proportion to the symptoms. In severe cases, the variation will be great, while in mild cases the rate and the symptoms will run almost parallel. When the disease reaches its height, there comes a time when the rate runs about parallel with the symptoms. As the disease begins to improve the rate drops more rapidly than do the symptoms. In cases having frequent exacerbations, the rate may be normal or below normal in the interval although the symptoms are present continuously.

Results of Hyperplastic Goiter.— Following an attack of hy-

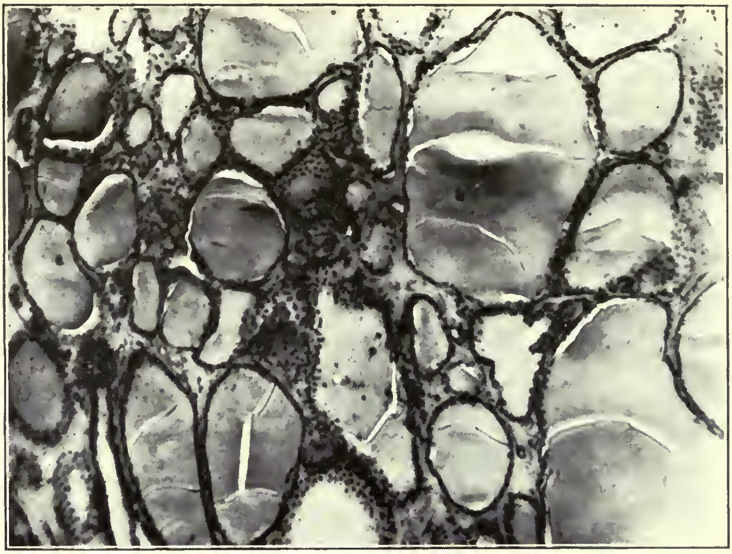


FIG. 7. COLLOID OR ADULT ADENOMA.

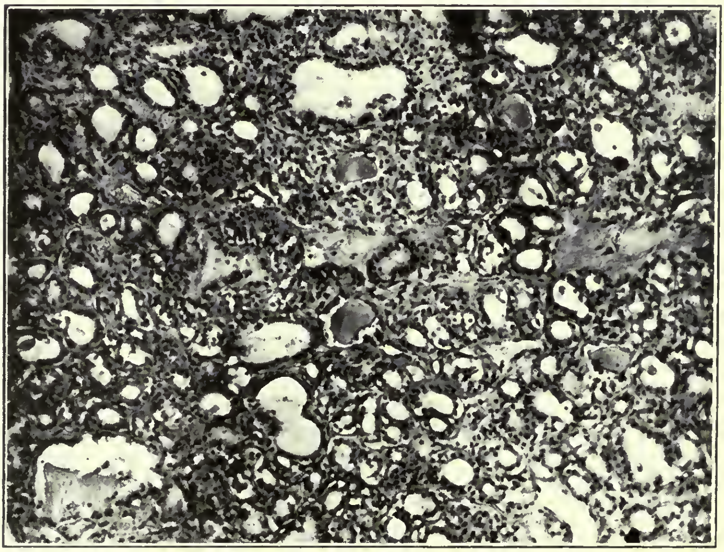


FIG. 8. MIXT ADENOMA.

perplastic goiter, there are 6 possible terminations: 1, Complete recovery, in which the rate becomes normal and the symptoms disappear. 2, Stage of remission, in which the symptoms persist, but the basal metabolic rate is usually within the normal limits or slightly below. 3, Partial remission in which there is not only a persistence of the symptoms, but also an increased rate, indicating that there is a continuous oversecretion. 4, Complete recovery so far as the thyroid gland and its secretions are concerned, as evidenced by a normal basal metabolic rate, but a persistence of certain of the symptoms, such as a rapid heart, exophthalmos, tremor, and mental irritability, because of permanent lesions produced by the action of the thyroxin. 5, Hypothyroidism, due to overdestruction of the secreting cells in the stage of retrogression. In this condition, the basal metabolic rate is below normal. 6, Hypothyroidism, with symptoms of hyperthyroidism. The former is due to overdestruction of epithelium or its inability to secrete sufficient thyroxin, and the latter is due to permanent lesions produced by the thyroxin in the height of the disease.

Cardiovascular Goiter.— Cardiovascular goiter is a clinical but not a pathologic entity, as it may be due to at least 3 different pathologic processes, viz., adenoma, adenomatosis, and regenerative or compensatory hyperplasia. The adenomata are new growths within a capsule, and may be single or multiple. There are 3 different varieties, the early or fetal, the late, called colloid or adult, and the intermediate or transitional stage, spoken of as the mixed. In the fetal adenomata, (Figs. 5 and 6)* the acini are at first small, without lumina, and lined with spheroidal epithelial cells. Later the cells become more cuboidal, begin to secrete colloid material, discharging it in a central direction, thus separating the cells and forming a lumen. The colloid secretion may continue until the acini become even larger than normal. In this case, the epithelial cells become flattened out similar to those seen in colloid goiter. This latter condition is known as the colloid or adult adenoma (Fig. 7). In the mixt state, (Fig. 8) both fetal and adult acini are to be found in large numbers. In the colloid or adult adenoma, there are always some fetal acini present. In the adenomata producing toxic manifestations, the evidence of degeneration is often present. However, it is not always present, and degeneration may be present without symptoms being produced.

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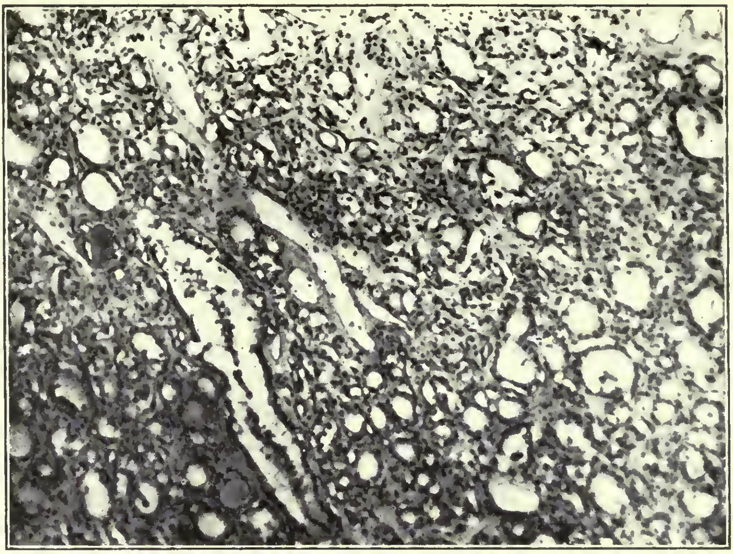


Fig. 9. Adenomatosis.

Fig. 10. Compensatory Hyperplasia.

Adenomatosis.— Adenomatosis (Fig. 9) is a diffuse growth without a capsule, which microscopically resembles the adenomata, particularly the mixt type. Like the adenomata, one can not tell from the microscopic appearance whether the condition was toxic or not.

The regenerative or compensatory hyperplastic type (Fig. 10) is one in which the secretion has been below normal from any of the various causes, and a compensatory hyperplasia is set up in order to produce the needed secretion. The process does not stop when a sufficient number of new acini to meet the needs of the body have been formed, but continues until there is an overproduction, and the patient becomes toxic. Compensatory hyperplasia occurs more frequently in colloid goiter than in any other deficiency lesion, but it may occur after any lesion that causes a deficiency in the amount of thyroxin produced.

Symptoms of Cardiovascular Goiter.— Altho cardiovascular goiter is not a pathologic entity, it is a clinical entity, as a similar clinical picture is produced by the various lesions. The symptoms are slow in developing and resemble those produced by other slowly administered toxines. Exophthalmos and the acute toxic symptoms seen in exophthalmic goiter, are absent. Tremor, tachycardia, mental irritability, loss of strength, and cardiovascular changes are present, but develop rather slowly. Cardiac hypertrophy is often greater in the cardiovascular type than in the hyperplastic type. The blood pressure is often increased.

Absorption of Thyroxin.— The work of Kendall would seem to show that the thyroxin produced in the normal gland, exophthalmic or hyperplastic goiter, and in the group of lesions producing cardiovascular goiter is the same. The difference in symptoms between these two types of toxic goiter may possibly be due to the difference in the rate of absorption of thyroxin. Plummer and Wilson have shown that the time elapsing from the first evidence of hyperplastic goiter until the course has reached its height averages about 9 months, while in cardiovascular goiter the time elapsing from the first appearance of the goiter until the height of the disease is reached, averages about 14 years. This means that in the hyperplastic goiter there is a rapid absorption of thyroxin, while in the cardiovascular goiter the absorption is much slower. In poisoning by other toxic substances, the symptoms vary very much between the

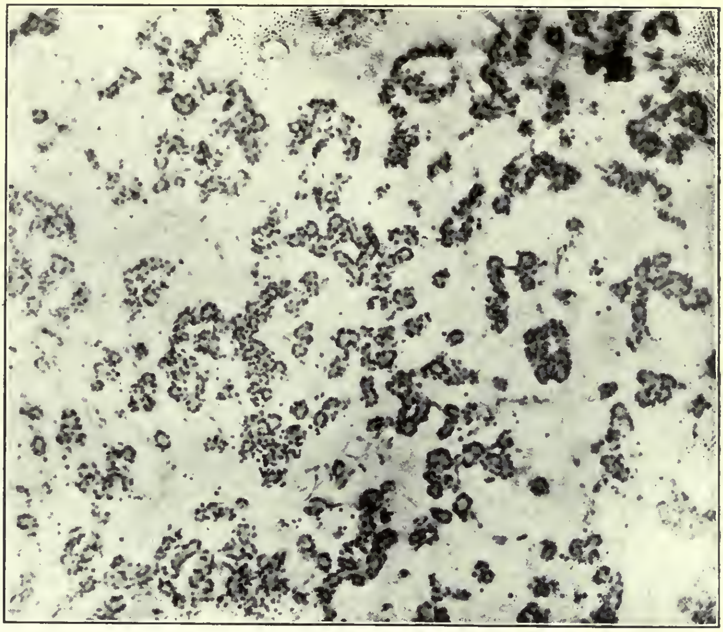


Fig. 5. Fetal Adenoma with Edema.

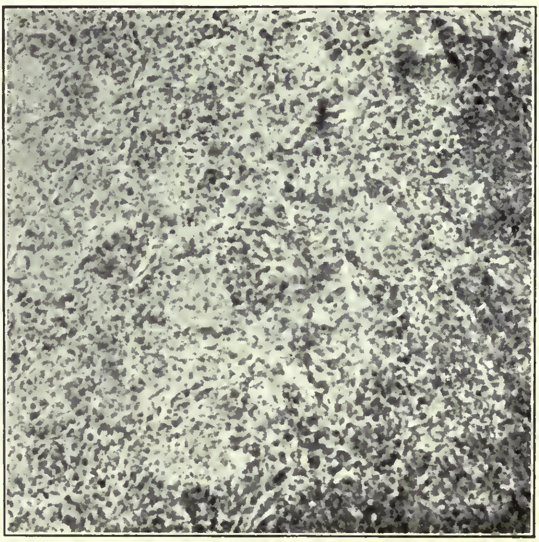


Fig. 6. Fetal Adenoma.

acute manifestation following a rapid administration of the poisonous substance, and the chronic manifestation following the slow administration, so that by analogy the explanation as stated would appear reasonable.

In cardiovascular goiter, the basal metabolic rate is an indication of the amount of thyroxin absorbed, regardless of the type of lesion. The curve rises much more slowly and usually does not reach so great a height as in the exophthalmic type. As a rule, cardiovascular goiter is not as severe as exophthalmic or hyperplastic goiter; but there are some very severe cases.

Permanent Lesions.— Permanent lesions may be produced by the action of the thyroxin upon the central nervous system, heart muscle, tissue back of the eyeball, or elsewhere, and thus after the thyroid secretion has become normal as a result of operation or resolution, the patient may still be irritable, have a tremor, a defective heart, a protruding eye, or other persisting manifestations. A patient may even develop myxedema, because of overdestruction of gland substance, and at the same time have some persisting symptoms of toxic goiter due to permanent lesions. These persisting lesions may be likened to the final results after an arm has been badly mangled. The bone heals, the soft parts heal, but the function of the arm may remain below par; so in some cases of toxic goiter, after the goiter has been cured, the symptoms persist because of irreparable lesions.

Basal Metabolism as an Indication to Diagnosis.— The diagnostic value of the basal metabolic rate may be summarized as follows: First, the basal metabolic rate is an indispensable index to the activity of the thyroid gland. Second, an increase in the secretion of thyroxin is followed by an early rise in the rate. This rise occurs before the clinical symptoms are manifest. Third, the height of the basal metabolic rate is not as important as is the course of the rate and the rapidity with which the rate is changing. Fourth, a rapidly rising rate or a rate that is higher than the symptoms would indicate usually means a rapidly secreting thyroid gland and greater severity than is seen with a slowly rising rate or a rate followed closely by the clinical manifestations. Rapid absorption following massage or surgical intervention must be excluded. Fifth, a stationary rate after a rise usually means that the disease has reached its zenith, but not necessarily so. Sixth, a falling rate indicates a decrease in the activity of the thyroid gland. A falling rate does not follow the activity of the thyroid gland as closely as does the rising rate, and neither is it followed as closely by the symptoms. Seventh, the variation between the falling rate and the symptoms is indicative of the intensity of the disease through which the patient is passing. The more severe the disease, the greater the variation. Eighth, a normal or subnormal rate, after an attack of hyperthyroidism accompanied by symptoms of the disease, is indicative of injury produced by the thyroxin. Often the injury is permanent, and the symptoms persist for life, although the patient may recover from the goiter so far as excess secretion of thyroxin is concerned. Ninth, a fluctuating rate after an attack of hyperthyroidism is indicative of pathologic activity, and exacerbations of more or less severe grade are to be expected.

Prognosis.— With a rising rate, a guarded prognosis should always be given. In general, with the first attack,when the rate is below 25 per cent. above the normal, the disease may be regarded as mild and the prognosis good; between 25 and 50% as moderate; between 50 and 75% as severe; and between 75 and 100% as very severe. The prognosis is grave if the rate is over 100%. A falling rate gives a much better prognosis than a rising rate.

Necessity for Correlation of Symptoms with Rate.— The character of the symptoms must always be considered in conjunction with the rate in determining the prognosis. In subsequent attacks, this is even more important than the primary attack. In permanent or persistent lesions, it requires but a small amount of thyroxin to produce a serious condition. Hence, the prognosis may be very grave even with a low rate. In other cases where there is a marked over-absorption of thyroxin as is evidenced by the high rate, the symptoms may be mild. It is not safe, however, to disregard the indication of the rate in the presence of mild symptoms, as these cases are apt to show very severe reactions. Neither is it safe to disregard the symptoms in cases where the symptoms are pronounced and the rate low, for fatal results may follow.

The Basal Metabolic Rate as an Indication for Treatment.— As has been stated before, the basal metabolic rate must never be taken alone, but only in conjunction with the clinical manifestations. In the onset of the disease with the rate below 25% medical treatment should be tried first. With a rate between

25 and 50%, the rapidity of the development of the disease together with the relationship existing between the rate and the symptoms are important factors. The rapidly developing disease had better be regarded as surgical. In the cases where the disease is advancing slowly, and the symptoms are developing as rapidly as the rate, medical treatment may be tried. In the developing disease with a rate not over 50%, the radical operation can usually be done without preliminary ligation. In cases seen in an exacerbation following the retrogressive stage, the symptoms of the patient are of great value in determining whether the preliminary ligation is necessary or not. Recurrent cases or cases in an exacerbation are always to be regarded as being surgical, altho the operation may need to be deferred.

With a rate between 50 and 75%, it is usually best to ligate the superior thyroid arteries and wait for the rate to drop before doing radical work. With a rate between 75 and 100%, radical work should never be done until the superior thyroid arteries have been ligated. In the majority of cases only one artery should be ligated at a time. It must be remembered in doing any work on the thyroid gland that the manipulation forces thyroxin into the blood stream. As a result there is usually an immediate rise in the rate followed by a fall in the rate. The interval that elapses between the operative procedures upon the gland should be great enough to permit the effect of the thyroxin thus forced into the blood stream to entirely pass away. For this reason the basal metabolic rate should always be observed after a ligation, and the next operation not done until the rate has ceased to drop. When the rate is over 100%, if the patient is in a precarious condition at all, no surgical work should be done, but the patient should be placed in bed, at absolute rest, and given sedatives and cardiac stimulants if indicated. With this procedure, the patient will usually improve and the rate drop to where a ligation is safe.

Undue stress must not be placed upon the importance of the basal metabolic rate, but its determination in the study and treatment of thyroid lesions should be as routine as are blood counts in infections. If this were done and the indications for treatment, as shown by a study of the basal metabolic rate in its relationship to the clinical symptoms, were followed, the operative death rate should be as low as that for the ordinary abdominal operation.

CHAPTER 19

THE METABOLIC RATE IN THYROTOXICOSIS[1]

By G. W. McCaskey, M.D.

Value of Basal Metabolism Determinations.— It may fairly be said that the basal metabolism test rests on an established scientific basis. The general physiologic and clinical significance of fluctuations in the metabolic rate is now also well understood. The next step is for clinicians to work out the range and value of their clinical application in suitably selected cases in routine diagnostic work. This is really the "touchstone" of any diagnostic method. Unless its clinical value can be shown to be commensurate with the time, labor and equipment required, it cannot and should not endure.

As an Index of Thyroid Toxicity.— The important question bearing on this clinical study is the dependability of fluctuations of the basal metabolic rate as an indication of thyroid activity; and this would obviously depend on whether the modified thyroxin molecule, if such exists, or possibly other unknown hormones, would retain the specific autocoid effect of the thyroxin molecule on cellular metabolism, or might possibly produce other toxic phenomena. Perhaps we cannot be too dogmatic on this point at present; but while recognizing the paramount position of the general clinical judgment in every case, variations in the metabolic rate as indirectly determined by the oxygen consumption must be regarded as the most scientific and practical index of thyroid toxicity.

As to the question, in what group or groups of cases are the routine determinations of basal metabolism worth while, I believe:

1. In all cases of definite goiter, and especially if associated with health disturbances, to ascertain the degree, if any, of its toxicity.

[1] Editor's abstract of "Basal Metabolism Determinations in General Internal Diagnosis", Jour. Am. Med. Ass., **74**:927-931, Apr. 1920. Abstract approved by author.

2. In a large group of cases either with or without goiter, with symptoms resembling, either closely or remotely, those of thyrotoxicosis.

In regard to the first group, whenever a patient has a goiter, large or small, and there is impairment of general health, whether the symptoms are typical of thyrotoxicosis or not, the toxicity of the goiter should be ascertained by the determination of the basal metabolism. This is especially true when considering the necessity for and character of therapeutic measures, surgical or medical. In any case with a goiter requiring a general diagnostic study, this accurate index of goiter toxicity should not be neglected. In judging of the operative risk in thyroidectomy, it is of the first importance. It appears to be true that this risk increases to an appalling degree when the metabolic rate attains an increase of around 100 per cent. Non-surgical measures should be exhausted in such cases in an effort to reduce the metabolic rate before operation, if the latter is decided on. The success of therapeutic measures can now for the first time be accurately gaged by basal metabolism determinations, instead of depending on the notoriously unreliable clinical data, such as pulse rate, or nervousness.

Equally important, and presenting great diagnostic difficulties, is the second group indicated. It does not matter much in the final judgment whether the patients have or have not a palpable thyroid. I have seen several cases in which the thyroid was very doubtfully palpable, with the metabolic rate increased more than 50 per cent.

Clinical Symptoms Suggesting Toxicity.— Much more important than the goiter is the history of the case and the character of the symptoms. Among the symptoms suggesting investigation along these lines may be mentioned:

1. Psychoneurotic disturbances.
2. Circulatory disturbances,
   - (*a*) Tachycardia or brachycardia.
   - (*b*) Cardiac myasthenias.
   - (*c*) Certain arrhythmias.
3. Fine tremors.
4. Hyperhidrosis and hypohidrosis.

5. General debility.
6. Loss of weight.
7. Slight temperature disturbances.

Not one of the foregoing symptoms can be regarded as strongly diagnostic, much less pathognomonic, of hypothyroidism or hyperthyroidism. In fact, it is perhaps not too much to say that if the majority or perhaps even all of these symptoms were present in an individual case, it would still be possible that the syndrome could be due to something entirely aside from thyroid disease.

Signification of Goiter.— As a matter of fact, if with these symptoms there are found a goiter and exophthalmos, the diagnosis of thyroid disease should be considered established. With the goiter alone this would not be so obvious, because if these symptoms, singly or collectively, can be due to causes other than thyroid disease, the presence or absence of a goiter would really prove nothing, altho creating a strong presumption in favor of hyperthyroidism or hypothyroidism to be verified by subsequent investigations.

Clinical Symptoms Versus Basal Metabolism.— It is probably unnecessary to comment at length on the individual symptoms enumerated above. Taking, for instance, such of the symptoms as psychoneurotic instability and tachycardia, which may be regarded as the most characteristic symptoms of the thyroid syndrome, it is perfectly obvious that they may be due to causes of the most diverse character. Nervous or mental overstrain, various chronic infections, but especially syphilis and tuberculosis, and a great variety of pathologic conditions occurring in the various glandular organs of the body, malnutrition, from whatever cause, gastro-intestinal disturbances, and many other conditions must be kept in mind as possible explanations of such a symptom group. Their differentiation from thyrotoxicosis can usually be made with a certain degree of probability by the general clinical picture and the usual diagnostic methods for the recognition of these pathologic conditions. The final court of appeal, however, so far as the thyroid problem is concerned, is the determination of the basal metabolism, which furnishes the most reliable proof either for or against the existence of thyroid disease.

Case Reports.— The following case reports have been selected because in them the metabolic rate furnished a more or less decisive factor in the diagnosis, which could not have been ascertained in any other way, thus illustrating the practical clinical value of these methods:

Case of Hyperthyroidism, with Chronic Hypertension.— *History.*— Mr. K., aged 43, complained of nocturnal asthmatic attacks. He had had an acute illness, diagnosed as pneumonia, one month before. One year before his health began to fail. He began to have some headache and to lose weight. He had lost 30 pounds during the last year. For the last two years, and probably for the last four years, he had had high blood pressure, ranging from 170 to 200, but he had been getting along fairly well until his acute illness one month before. The trouble began suddenly while he felt in good health. One evening he had a sensation of difficult breathing, with wheezing in the chest, which got so bad that medical aid had to be called. His physician found him with distressing asthmatic dyspnea, and this had recurred every night, becoming very severe at times.

Physical Examination: The pulse was 135, and regular. The systolic blood pressure ranged from 185 to 200, the diastolic from 130 to 145, indicating rather low pulse pressure. A systolic murmur was heard at the apex. There was an area of dulness over the manubrium. The urine showed some hyaline and granular casts, but the excretion of fluid and solids was within normal range. The blood was normal; the Wasserman test negative.

June 23, 1919, the blood sugar, fasting, was 0.014; August 7, 0.121; one hour after 100 gm. of glucose, 0.233; two hours after 100 gm. of glucose, 0.140.

Roentgen-ray examination revealed definite dilatation of aotic arch, and enormous enlargement of the heart.

June 3, six days after the first examination, the basal metabolism was + 50 per cent; July 3, + 70 per cent..; August 5, + 97 per cent. There was a distinct gallop rhythm.

The patient died October 13.

This case is one of extraordinary scientific and clinical interest. Under rest and varied drug treatment the dyspneic attacks disappeared and the patient improved clinically in every respect. It will be noted that the basal metabolism at the outset indicated a moderate grade of thyrotoxicosis, which it was thought would yield under treatment. No goiter could be detected by us or by the clinicians at the Mayo Clinic, where the patient went later for an examination. He had, however, a very short, thick neck, and a goiter of considerable size might have escaped detection. The subsequent marked increase in basal metabolism is thus best explained by increasing thyroid toxicity. The case was such a typical one of chronic hypertensive cardiovascular disease that the thyroid factor would be pushed entirely into the background unless forced to the front by the basal metabolism determinations. The etiologic relationship of the thyrotoxicosis to the cardiovascular disease could not under the circumstances have been determined, but a careful study of the case suggested, on the one hand, the possibility just indicated, and, on the other hand, the desirability of carefully studying the basal metabolism in chronic hypertensive cases to determine the possible evolution of thyrotoxicosis.

Case — Hyperthyroidism, Syphiliphobia.— *History:* Mr. S., aged 31, complained of being nervous and restless, and was always tired in the morning on rising. He had been "doctoring" for the past seven or eight years. He had had some palpitation and dyspnea, and was fully convinced that he had syphilis.

Physical Examination.— This was negative, except for fine tremor. Repeated Wasserman tests (four) were negative. The blood sugar, fasting, was 0.079; it was 0.152 one hour after 100 gm. of glucose, and 0.162 two hours after 100 gm. of glucose. The basal metabolism was +41 per cent.

In this case the determination of the basal metabolism converted a syphiliphobic patient into a thyrotoxic one, from the standpoint of diagnosis.

In conclusion, I wish to say that so far as I am concerned, the procedure of establishing the metabolic rate in cases indicated has passed the experimental stage and has been assigned its place in my diagnostic armamentarium to be used as occasion requires.

CHAPTER 20

TREATMENT OF CERTAIN TYPES OF GOITER[1]

By Stuart McGuire, M. D.

The Role of the Thyroid.— The thyroid is in many respects the most wonderful organ in the body. Thru its internal secretion it influences the physical development of the child and the mental activity of the adult. It regulates the growth of bone, the formation and distribution of fat, and the nutrition of the skin, teeth, hair and nails. It plays an important part in menstruation and parturition and has much to do with sexual desire and power. It influences the rate of the heart beat, the character of the peripheral circulation, and hence markedly affects the general blood pressure. It presides over the nitrogenous metabolism of the body and in other, and perhaps unsuspected ways, plays an important part in the human economy.

If thyroid secretion is excessive there are symptoms of metabolic riot. Heat production and gaseous interchange are rapid. The body tissues are stimulated to a course of wasting dissipation. There are seen tremors, sweating, tachycardia, muscular weakness, loss of weight and feverish mental activity.

If thyroid secretion is deficient, the metabolism of the body is depressed and heat production and gaseous interchange are at a low ebb. In the young, growth is lessened and the skeletal system is dwarfed. Connective tissue cells remain myxomatous. The skin is dry and thick and the hair coarse and shows deficient nourishment. The nervous system halts in development and mentality does not rise above the level of the infant.

Relation of Metabolic Rate to Thyroid Gland.— It has been learned that the thyroid regulates the general metabolism of the body and that an increase or decrease in its activity is accurately shown by corresponding changes in the patient's metabolic rate. Hence, by determining the degree of metabolism, we now

[1] Editor's abstract, "Treatment of Certain Types of Goiter," Virginia Med. Monthly, Jan., 1921. Approved by author.

have a scientific means by which we can estimate thyroid activity in an individual case, and can tabulate mathematically the effect of the various forms of treatment that are advocated for its abnormalities.

The exact clinical value of the metabolic rate is yet to be determined. Like the thermometer, it promises to be a most valuable agent, but also like the thermometer, its record must be considered together with the patient's clinical symptoms.

Types of Thyroid Disease.— Disease of the thyroid usually results in perversion of its function. If it causes diminished thyroid secretion the condition is known as hypothyroidism. If it causes increased secretion it is known as hyperthyroidism. Enlargement of the thyroid gland is termed goiter. If it be due to a general increase of tissue it is called a parenchymatous goiter. If due to the growth of a tumor it is called an adenomatous goiter. If due to the retention of secretion it is called a cystic or colloid goiter. Often two, or even all three of the above conditions may be found in the pathologic study of a single specimen. A goiter that causes no perversion of thyroid function and merely produces mechanical symptoms is called a simple goiter. This clinical division is not a hard and fast one, however, because a simple goiter may take on activity and cause general symptoms, and a toxic goiter may undergo degenerative changes and cease to produce constitutional disturbances.

Treatment of Various Types of Goiter.— The treatment of simple goiter permits of little discussion. The parenchymatous type which causes the symmetrical enlargement of the thyroid, so frequently seen in girls about puberty, tends to spontaneous cure and is benefited by improving the patient's hygienic conditions and by the internal administration of thyroid extract and the external application of tincture of iodin. The adenomatous and colloid types are not influenced by treatment. They may later develop toxic symptoms, or undergo malignant degeneration, but as a rule they simply cause deformity and pressure symptoms. The patient is often the best judge as to when the disfigurement or discomfort they produce is sufficient to justify an operation. Toxic goiters are much more serious and should be treated early and by efficient measures.

While we do not know much about the etiology of exophthalmic goiter, it is a fact that the condition frequently follows some acute disease and is maintained by a local focus of infection. Before beginning the systematic treatment of any case the tonsils and teeth should be examined and other possible sources of poison such as intestinal stasis should be determined, and if any diseased condition is discovered it should be corrected.

Rest.— Rest is the first and most essential factor in the medical treatment of the disease. It should be absolute and complete and must be mental as well as physical. It is useless to try to secure it at home. The patient should be placed in a hospital where he can be under proper control. Means and Aub studied the effect of rest on a group of cases. These patients had an average metabolic rate of plus 81 per cent. and after one to three weeks the same group had an average of plus 67 per cent. In a few of the more toxic cases the curve rose in spite of rest. There was no case in the series whose metabolism was brought to within normal limits by rest alone. After a certain time a level was usually reached and rest alone did not cause a further drop.

Drugs.— The administration of various drugs with a view to lessening metabolism has been advocated. Of these, hydrobromate of quinine with ergotine, glycholate of soda and pancreatic extract have the greatest number of advocates. Means and Aub have tested the action of hydrobromate of quinine on a group of patients and found that with these cases it had no apparent effect on the metabolic rate.

X-Ray.— The use of X-Ray has long been advocated, and more recently the application of radium has been recommended, the theory being that a sclerosis is produced which lessens glandular activity. The relative merits of X-ray and radium have not yet been determined, but it seems that the choice is largely a question of the experience of the operator and the convenience of the patient. Means and Aub tested the effect of X-ray on a group of cases. These patients had an average metabolic rate of plus 63 per cent. After one or two treatments at intervals of one month, there was a reduction to plus 52 per cent. After four or five treatments there was a reduction to plus 40 per cent., and after two or three years' treatment there was a reduction to plus 13 per cent. and the patients were able to lead normal lives. The advantages claimed for the X-ray method of treatment are that it avoids an operation and is attended by less danger to life. The disadvantages are the increased length of invalidism, the greater difficulty of operating if surgery is ultimately necessary, the possibility of shrinkage of tissues of neck, danger of myxedema and of X-ray burns, and the liability of treating colloid and cystic goiters which are not benefited.

Boiling Water Injections.— The injection of boiling water or a solution of quinine and urea into the body of the thyroid has been advised in the initial stages of hyperthyroidism, and as a preparatory measure to partial thyroidectomy in patients too ill to warrant any form of immediate operative procedure. The theory on which this practice is based is that the destruction of glandular cells and the obstruction of blood vessels will cut down the output of thyroid secretion. The method has many enthusiastic advocates who report good results. It is not without immediate or remote disadvantages and dangers. Some patients are so sick that even this apparently simple procedure will cause an acute and perhaps a fatal hyperthyroidism; others will not be benefited, and a subsequent surgical operation will be made difficult by the adhesions it has caused, and finally the irritation may eventually result in the development of cancer.

Surgery.— It is generally conceded that at present the safest, surest and most satisfactory treatment of hyperthyroidism is surgery. The practice of destroying a part of a gland in order to lessen its physiological activitv is certainly illogical, and only defensible on the ground that we are confronted with a condition and not a theory. Still it is a fact that while a patient is benefited by rest and drugs, and sometimes either makes a spontaneous recovery or is cured by repeated and long-continued X-ray or radium treatment, he is given his best chance by an operation, and in order to economize time and avoid the possibility of serious complications, one should be advised as soon as the diagnosis of the disease can be established by the clinical symptoms, the metabolic rate and the Goetsch test.

Ligations.—The operations performed for hyperthyroidism are ligations and partial thyroidectomies. The benefits from ligations are marked but the results are rarely permanent. Observation in a series of cases at the Mayo Clinic showed that ligations reduced the metabolic rate from an average of plus 57 per cent. before operation to an average of plus 39 per cent. three months after operation and there was also a corresponding improvement in clinical symptoms and an average gain of 21 pounds in weight. Experience has proved, however, that sooner or later there will almost invariably be a relapse and the patient's condition become worse than before. Ligations, therefore, are not relied on to effect a cure but are employed either as a test of a patient's reaction to trauma in cases where there is doubt of the individual's ability to stand a thyroidectomy, or as a means to get a patient in condition for a more radical operation when it is obvious that at the time a thyroidectomy could not be done without great hazard.

Partial Thyroidectomies.— The results of partial thyroidectomies are prompt and permanent. If the operation does not effect a satisfactory cure it is because either not enough of the gland has been removed, or the operation has been delayed until the patient's symptoms are no longer due to hyperthyroidism alone but to organic changes in the vital organs as well. Means and Aub found in a group of cases that the average metabolic rate was plus 46 per cent. before thyroidectomy and during the first two weeks after the operation there was a fall to plus 21 per cent. To get the best results it is necessary to remove the major portion of both lobes and the isthmus of the thyroid, leaving only a small amount of tissue cut from the posterior border of the lobes to carry on the function of the gland. This safeguards the para-thyroids and recurrent laryngeals and gives a symmetrical neck. Acute post-operative hyperthyroidism, which is the greatest danger of the operation, is not due as much to the amount of the gland taken out as it is to the amount of the gland left in. When it develops to a dangerous degree, the treatment advised by Crile of packing the patient in ice will be found most efficacious.

CHAPTER 21

DIAGNOSIS OF PSYCHONEUROSIS AND TRUE HYPERTHYROIDISM IN THE EX-SERVICE MAN

BY CARMEN F. JAMES, M. D.

Approved for publication by the Surgeon General of the U. S. Public Health Service.

Prevalence of Neuro-Psychiatric Cases.— The recent war has brought to the attention of the Medical profession an alarming number of neuro-psychiatric cases. The Government agencies dealing with the ex-service men have announced that they need nearly as many beds for neuro-psychiatric cases as for tubercular, and far more than for all other classes of cases combined. This is a significant question and invites consideration.

Is the War Responsible?— The war itself probably was not the primary causative factor in the production of more than a few neuro-psychiatric individuals. A few who were pronounced neurasthenics were taken into the Service under the stress of enlistment or by the draft boards. In the greater number of cases, by far, the war was merely the immediate provocative cause, based on a congenital neuropathic or psychopathic personality. The most of these men have had, practically all of their lives, an unstable nervous system. Some had had more or less symptoms before service. This did not materially interfere with their activity or usefulness. There were others who had had no recognizable trouble prior to the war. The excitement of going to camp, the change in the daily routine and habits of their life, and the new and unusual requirements of military life had a detrimental effect on this unstable nervous system. Some of these developed marked signs of "shell shock" without ever leaving the United States or hearing a gun fired. There were others that did not break until they were subjected to the strain of actual campaigning at the front. Some of these cases were very severe, and required removal from the lines and intensive treatment at the hands of specially trained workers. Others were mild and did not prevent the soldier from continuing his duties with his detachment.

Problems of Differential Diagnosis.— With the close of the war and the return of these men to civil life, the physicians in civilian practice as well as the Public Health personnel have had to care for many of these disabled men. Many problems of differential diagnosis present themselves to all of us. Some are easy of solution but others are very difficult. Some of these cases are at first confused with pulmonary tuberculosis, heart disease of various types, hyperthyroidism or goiter, gastro-intestinal conditions, organic disease of the central nervous system, and many other conditions not necessary to mention. On first thought it may seem strange that this confusion should occur, but most all of us can recall numbers of such mistakes in our own experience. We frequently have to call into play our highest skill in diagnosis and make use of the best methods of precision of the laboratory, and even then we will at times make mistakes.

We are concerned mainly in this article with those cases of psychoneurosis that resemble hyperthyroidism, and more especially the value of the study of the basal metabolic rate in differentiating these cases from true hyperthyroidism. The opinions expressed in this article are based on observations made on ex-service men while the writer was stationed at the U. S. P. H. Hospital No. 36, Boston, Mass.

Symptoms Common to Psychoneurosis and Hyperthyroidism.—Among the ex-service men, and it is equally true in civilian practice, we sometimes see a type of psychoneurosis that resembles, in many respects, hyperthyroidism, and occasionally even exophthalmic goiter. They present an unstable nervous system that reacts unduly to minor stimuli. There is usually a tremor of the outstretched fingers and protruded tongue, and even of the entire body in some cases. These tremors vary in degree from very mild to very severe. They are more often coarse in character, and usually accentuated by directing attention to them. They can usually be lessened or made to disappear by diverting the patient's attention during the examination.

These patients nearly always have an accelerated pulse rate, ranging around 100 per minute. The rate, however, is very variable, and the heart responds in a marked degree to very mild stimulation, such as slight amount of excitement, exercise, or emotional disturbance. The patients are conscious of this, and frequently complain a great deal of palpitation, shortness of breath, vague pains in the cardiac region, and even attacks resembling angina pectoris, as in one of my cases. The pulse rate in these cases is influenced readily by complete rest, usually dropping to below 90, or even to normal. This drop is slight in cases of true hyperthyroidism.

Some of these patients may show slight evidence of the other cardinal symptoms of exophthalmic goiter — exophthalmos and enlargement of the thyroid gland. These are incidental and have no causation in the nervous condition. You may sometimes see a mild hyperthyroidism in a marked psychoneurotic. Some even contend that all the cases of the type under discussion have their origin in a disturbed thyroid secretion. Yet we see some cases in which there appear to be a slight exophthalmos and enlargement of the thyroid gland, along with a tachycardia and nervous manifestations when the basal metabolism rules out absolutely any hyperfunction of the gland.

Quantitative Test for Thyroid Activity.— The basal metabolism determination is the only practical method of precision that the laboratory has developed that can be used as a measure of thyroid activity. It is of value in thyroid disturbances in that it is a measure of the basic metabolic activities taking place in the body. These activities are so closely linked with the thyroid secretion that it may be, for all practical purposes, considered a measure of thyroid activity. It is the only quantitative test we have for thyroid hyperfunction. It has been conclusively shown by many of the workers in metabolism[1] that the basal metabolic rate fluctuates according to the degree of activity of the thyroid gland. When the symptoms in the hyperthyroid case increase in severity, the basal metabolism shows a corresponding rise in rate, and as the condition improves under treatment the metabolism rate drops accordingly. Consequently it is of great value in diagnosing disturbances of thyroid activity, and following accurately the patient's condition while under treatment. It is also especially valuable in differentiating from

[1] Means, J. H.: Hyperthyroidism (Toxic Goiter), Medical Clinics of North America, January, 19 20.

Du Bois, E. F.: The Basal Metabolism as a Guide in the Diagnosis and Treatment of Thyroid Disease, Medical Clinics of North America, **2**: 1201, January, 1919.

Boothby, W. M.: The Value of the Basal Metabolic Rate in theTreatment of Disease of the Thyroid, Medical Clinics of North America, November 1919.

srue hyperthyroidism many of those borderline cases that re-temble hyperthyroidism. This is its value in a neuro-psychiatric clinic.

Goetsch Test.— A few years ago the Goetsch[2] test was introduced as a simple diagnostic test for hyperthyroidism. This was soon shown not to be specific in nature, and the results not to be sufficiently uniform for practical use. A large percentage of neurasthenics show a marked positive adrenalin reaction. Peabody[3] and his associates found a positive Goetsch test in 60 per cent. of cases of "irritable heart" in soldiers examined by them. O'Hare[4] found positive reactions in cases of hypertension. Russell, Millet, and Bowen[5], in a comparison of the functional tests for hyperthyroidism, found the adrenalin test positive in 55 per cent. of their cases of hypothyroidism, and negative in 2 cases with basal metabolic increase of over 50 per cent. Consequently this method has been discarded because it is unreliable.

Conclusions.— The value of the basal metabolic rate in thyroid disturbances is too well established to be questioned. It is equally valuable in the study of those borderline cases resembling hyperthyroidism, such as certain cases of neurasthenia. The results are quite clear. The hyperthyroidism gives an increase in basal metabolic rate, the neurasthenia does not. Most of us have had the experience of diagnosing "irritable hearts" and neurasthenias as hyperthyroidism until the basal metabolism was determined and compelled us to change our diagnosis. Indirect calorimetry has been developed and simplified to such a point that it has become comparatively easy to obtain results sufficiently accurate for clinical purposes. With the increasing use of the apparatus for determining the metabolic rate, fewer errors in diagnosis will be made.

[2] Goetsch, E.: Newer Methods in the Diagnosis of Thyroid Disorders, Pathological and Clinical, New York State Medical Journal, **18**: 7, July, 1918.

[3] Peabody, F. W., Clough, H. B., Sturgis, C. C., Wearn, J. T., and Tompkins, E. H.: Effects of the Injection of Epinephrin in Soldiers with "Irritable Heart", Jour. Am. Med. Ass., Dec. 7, 1918.

[4] O'Hare, J. P.: Vascular Reaction in Vascular Hypertension, American Journal of the Medical Sciences, **159**: 369, March, 1920.

[5] Russel, N. G., Millet, J. A. P., Bowen, B. D.: Clinical Studies in Functional Disturbances. Study 1. Functional Thyroid Tests as an aid to Differential Diagnosis, American Journal of the Medical Sciences, **162**: 597, Dec., 1921.

CHAPTER 22

HYPOTHYROIDISM — PHYSIOLOGICAL, PRIMARY, AND SECONDARY

By Edwin L. Gardner, M. D.

Definition.— Hypothyroidism is a condition produced by an impairment of the function of the thyroid gland and characterized by a retardation of cellular metabolism and growth.

Classification:—

Physiological Hypothyroidism:
- *a*. Estimation of thyroid function.
- *b*. Effect of diet.
- *c*. Other physiological conditions.

Primary or Congenital Hypothyroidism:
- *a*. Cretinism
- *b*. Minor Congenital Hypothyroidism

Secondary Hypothyroidism:
- *a*. Following Hyperthyroidism
- *b*. Following surgery upon the thyroid gland
- *c*. Thyroid deficiency associated with disease of other endocrine glands
- *d*. Following removal of other endocrine glands
- *e*. Myxedema. Its Symptoms
- *f*. Minor thyroid deficiencies
- *g*. Following infections and toxemias

Treatment of Hypothyroidism
Physiological Hypothyroidism

Estimation of Thyroid Function.— The clinical estimation of thyroid function is often uncertain. The observations and experiments of Plummer and associates suggest an equilibrium between the "thyroxin" in the thyroid gland, the blood, and the tissues of the body. The thyroid principle is probably used as a catalase, acting as a stimulus which controls cellular metabolism. It is not absolutely necessary for life, but in order to have the greatest efficiency, the total amount may vary within comparatively narrow limits. These facts afford some basis for studies of basal metabolism in thyroid disease. Much has been written and said about the technic and value of basal metabolism; unfortunately many good clinical men are doubting its accuracy and value. It is a procedure in which extreme care must be employed in controlling the technic and in the interpretation of the results. If the test is made by a trained technician and intelligently interpreted, it furnishes information which nothing else will. There are limitations, such as urine analysis has in urinary disease or the Wasserman test in syphilis, but nobody would wish to discard either of these last well-known and accepted laboratory examinations. Much error has arisen over the fact that other conditions than gross or microscopic thyroid disease may affect the basal metabolic rates. To assume that all cases coming within the limits of plus or minus 10% or any other figures, are normal, and that patients having a rate above or below are abnormal, can not be entirely supported by clinical observations. Repeated observations of the same patient, whether normal, hyperthyroid, or hypothyroid, will show considerable daily or even hourly variation, but the curve will be *essentially a normal, hypothyroid or hyperthyroid type.*

Effect of Diet.— Many conditions have a tendency to cause slightly lowered basal metabolic rates and the borderline between the physiological and pathological states can be determined only by the associated clinical symptoms and findings. Animals have shown lowered rates when on insufficient diets. Hibernating animals have a metabolism much below the normal and the iodin content of their thyroid glands is low in the spring months. Cattle, sheep and hogs killed early in the spring show a very low iodin content of their thyroid glands. It is uncertain whether this is due to seasonal or to dietary influences, but the latter is most probable. Pregnant sows fed upon iodin-poor food frequently abort or give birth to hairless pigs with brittle hoofs, and enlarged thyroids; an observation which has been most common in spring months.

Other Physiologic Conditions.— It is a common observation of clinicians to note that patients are very susceptible to infections, if the diet is poor in those active principles called vitamines, altho the patient may be well nourished and apparently healthy. The basal metabolic rate may be lowered

20% below normal in malnutrition cases; this has especially been noted in the starvation treatment of diabetes. Heavy feeders, especially of meats, very commonly fall in a class slightly above normal. Pregnancy is not uncommonly associated with mild hypothyroidism; and following periods of nervous strain and excitement, when signs of "physiological hyperthyroidism" are present, the basal metabolic curve may temporarily drop below normal. Old age is usually associated with rates below normal, and often many of the symptoms and findings of old age have been attributed to hypothyroidism. Symptoms of hypothyroidism are very common in women following the menopause. These patients rapidly increase in weight and sometimes show signs of early myxedema.

Primary or Congenital Hypothyroidism

Cretinism.— True cretinism is always congenital, altho clinically, infantile myxedema developing before the end of the first year of life can not be differentiated from it. After the first year of life, infantile myxedema may usually be recognized when ossification has proceeded to the stage of closure of the fontanelles. Infantile myxedema in the first years of life shows many of the same manifestations as true cretinism and for practical purposes the two conditions may be grouped together. The classical clinical picture is well known and is well described in most of the textbooks.

Minor Congenital Hypothyroidism.— Altho typical cretinism or myxedema in childhood once recognized can never be forgotten, minor hypothyroidism may occur and escape detection. This condition usually occurs in backward or abnormal children and is often associated with other abnormalities. Delayed bony ossification, indicated by failure of closure of fontanelles; slowness in learning to walk; delayed eruption of teeth with malformation and early decay; malformation of bones of the face with high palate and poor development of the nasal cavity; spinal curvature and possibly the tendency to rickets may be associated with thyroid deficiency. Puffiness and dryness of the skin, large abdomen, small, weak muscles, tendency to lymphatic hypertrophy, poor growth of the hair, retardation of mentality, sleepiness, anorexia, lowered temperature, atonic constipation, enuresis and many other symptoms due to a slowing up of cellular and nervous activity are suggestive when groups of symptoms appear together. No single symptom or even group of symptoms is pathognomonic, but should be investigated and checked by the therapeutic test with thyroid extract.

Patients with other endocrine gland disturbances may show symptoms of abnormal thyroid function. Older children with persistent thymus, tendency to lymphatic enlargement, susceptibility to infections, and possibly findings referrable to pituitary and sexual glands, show mild thyroid deficiency. Many of these cases have a lowered basal metabolic rate, and improve considerably under prolonged feeding of small doses of thyroid extract, sufficient to maintain the rate nearly normal.

Secondary Hypothyroidism

Following Hyperthyroidism.— The hyperthyroid state very commonly passes gradually into one of lowered function. It can not, without reservations, be assumed that a thyroid disturbance is a quantitative one only. Dysfunction may play an active part. The study of creatin and creatinin metabolism, the study of blood sugar, and many of the clinical signs suggest a qualitative alteration of thyroid secretion. Much of the pathology resulting from the hyperthyroid condition remains permanent and confuses the picture.

Following Surgery.— Myxedema or minor hypothyroid states often follow surgical procedures on the thyroid glands. Resection, X-Ray, or injection of foreign substance, all may result in too low activity, due to reduction of thyroid substance.

Associated with other Endocrine Diseases.—The thyroid syndrome is always complicated by those signs arising from other glands of internal secretion. Pituitary disease affects thyroid function. Activity of the gonads materially influences thyroid function and menopause is not uncommonly followed by minor thyroid deficiency or myxedema. Removal of a fibroid uterus or oophorectomy, may be followed by hypothyroidism.

The largest number of cases arises from insidious or unknown causes. Infections and toxemias probably produce a large group of cases, due to atrophy or sclerosis. Vascular disease (old age) possibly is a factor in a small number of cases. Many of the patients with hypothyroid disease, may have been "thyroid poor" at birth.

Myxedema.— A case of true myxedema can not be mistaken, when once a few cases have been recognized. However, it is not uncommon to find myxedema patients who have been treated for nephritis, cardiac disease or other ailments. The symptoms and signs of myxedema are varied, due to the altered cellular metabolism. Myxedema (Gull's disease) is more common in women than men. It is more likely to occur in families who have thyroid or other endocrine gland disturbances, and is more common in goitrous communities. The disease may first appear in relation to pregnancy or menstruation, and after partial remissions become permanently established. The symptoms may be referred to various organs:

A characteristic infiltration of the skin is due to a substance resembling mucus, and a formation of new connective tissue. The skin of the entire body may be affected, but is more likely to appear in certain areas, as the face and neck, supraclavicular fossae, breasts, the wrists and back of hands, and about the ankles. The skin is often dry and scaley, and frequently tender upon pressure. The nails are dry, the hair coarse and has a tendency to fall out, especially the lateral portion of the eyebrows. The hands are often "spade-like" and movements are clumsy. The face has a mask-like expression, the eyelids are swollen, and patches of pigmentation frequently occur about the face, forehead, or neck. The mucous membranes show a similar process. The tongue is thickened, the conjunctiva often inflamed, the gums are swollen and pyorrhea is very common. Thickening of the mucosa of the larynx causes a peculiar monotone to the voice. Tonsils and adenoids are common, and the patients often suffer from tinnitus and partial loss of hearing. Various symptoms may be produced from infiltration of the mucosa of the gastrointestinal, bronchial, urinary and genital tracts.

Some symptoms are due to retardation of ossification if the disease appears early in life. This is especially noted in disease of dentition in young people. There is a tendency to early caries of the teeth. Fractures heal poorly. Infiltration of the cartilages may produce pain, stiffness and creaking about the joints, and especially so about the knee joints. The muscles are flabby and weak; muscular movements are slow and fatigue quickly appears.

The pulse is often slow, small and of low tension. Arterial degeneration may appear early. The heart dilates to the right and to the left and the electrocardiogram shows many signs of impaired myocardial function.

A moderate anemia is the rule. The leucocyte count is usually reduced and there is a lymphocytosis. A tendency to hemorrhage may exist, especially of the purpuric type.

Anorexia is common and sensation of thirst is decreased. The general suppression of cellular activity is likely to produce atony, achylia and subsequent disturbances of motility and digestion. The liver may be enlarged and the function impaired.

The function of the kidneys is impaired, as shown by decreased urine output, albuminuria, and often casts. Frequent urination or incontinence may be present either due to myxedematous infiltration or to infection. Enuresis in children sometimes responds to thyroid extract.

Arrested development occurs if the thyroid deficiency develops early in life. Menorrhagia may appear, or there may be atrophy of the genitals with a premature climacteric. Some believe sterility may be associated with subthyroidism.

Susceptibility to respiratory infections is common and dyspnoea is often present. The dyspnoea may even be mistaken for bronchial asthma.

The nervous symptoms are most marked in myxedema. All mental processes are slowed up and fatigue appears early. Memory is slow and less often markedly impaired. Sleepiness is the rule, but little relief is obtained from many hours of rest and sleep. Headache is common and the patients show signs of mental irritability and depression. Melancholic symptoms are not uncommon. Nervousness and tremor may appear and occasionally syncope or even convulsive seizures may be present. All movements are clumsy. Infiltration of the peripheral nerves may produce symptoms.

Minor Thyroid Deficiency.—Minor thyroid deficiency is much harder to recognize and as a rule can only be suspected. The therapeutic test is usually employed. The estimation of basal metabolism has made the diagnosis much more certain, but not infallible. Lowered metabolic rates are common but the statement that they run parallel with thyroid function probably is not justifiable. The greatest discrepancies appear through slight errors in technic, but other factors may materially affect the results. The majority of myxedematous patients have a rate of 20% to 40% below the normal, but some malnutrition cases will reach 20% below normal. Some patients with symptoms and findings suggesting minor hypothyroidism will show a curve only by repeated examinations which is definitely below the normal limits.

The writer has recently studied 275 cases who had a basal metabolic rate varying between 0 and 40%. These were mostly ambulatory patients in whom some thyroid or other endocrine gland disturbance was suspected; about 40% of the cases were patients with malnutrition and a few were indefinite "neurasthenic" individuals. A few normal people were included in the group but none of these had a rate below 5%. Females outnumbered males 6 to 1. Thirty-four patients were under 20 years of age. The majority of these 34 cases had goiters of adolescence, a few were girls with various nervous symptoms associated with delayed menstruation, and the others had multiple endocrine gland disturbances. All showed improvement after the administration of iodides or thyroid extract, with the exception of some of the multiple endocrine gland cases. One child suffering from polycythemia associated with large spleen and cirrhotic liver showed marked improvement.

Malnutrition caused a lowered metabolic rate in 40% of the cases studied. Of 53 patients in the third decade of life, all except five had to be placed in this group; two had had a previous thyroid operation, two ovarectomy, and one a premature menopause of unknown cause. Myxedema and minor hypothyroidism appear most commonly in the fourth, fifth, and less often in the sixth decades of life. Malnutrition is only one-half as common; but menstrual disturbances, pelvic operations multiple pregnancies, and disturbances near the menopause occur more often. Several cases first showed symptoms after ovarectomy or removal of fibroids. Only 14 cases were over 60 years of age and only six of these showed signs of diminished thyroid function, the others were undernourished. Only ten cases of entire series showed typical myxedema. The basal metabolism was determined frequently and —10% seems as good as any arbitrary figure as a dividing line between the normal and 0, even in definitely thyroid deficient cases when only *one* estimation is made. The condition of the thyroid was noted in the majority of the cases. In myxedema and definite thyroid deficiency the gland most often shows signs of atrophy or sclerosis. In many of the minor cases, especially in young people, there was slight or moderate enlargement. About 50% of the cases had thyroids which clinically could not be differentiated from the normal.

Following Infections and Toxemias.— Experimentally hypothyroid animals are very susceptible to infections, in fact it is often hard to keep them alive long enough to carry out experiments. They show poor antibody formation. At least one investigator believes that the ability to produce antibodies may be exprest in terms of thyroid function; he claims to have increased the antibodies of the blood in poorly reacting animals by feeding thyroid extract. Cretins and myxedematous patients show very low resistance to infections. Following infectious diseases such as pneumonia, acute tonsillitis, typhoid fever, acute rheumatic fever etc., we have repeatedly found lowered basal metabolic rates, and convalesence very often was tedious; improvement was apparently faster in those whose metabolism quickly returned to normal limits. Many of the symptoms of convalesence such as subnormal temperature, slow pulse, lack of endurance, susceptibility to cold, tendency to atony of striated and non-striated muscles, rapid gains in weight, etc., might be attributed to lowered thyroid function, as a result of a generalized toxemia affecting all the cells of the body. Much of the old treatment of postinfective cases was directed towards increasing muscle tone and stimulating metabolism. No sharp line can be drawn between physiological depression of thyroid function and real pathological degeneration of the gland.

Diagnosis of Hypothyroidism.— It is not possible in all cases to decide whether the thyroid depression is the cause of the symptoms or whether it is a part of the generally lowered metabolism. Malnutrition and postinfective cases probably belong to the latter group. The following symptoms and signs justify the suspicion that subthyroidism may exist and basal metabolic studies should be made.

1. Lack of endurance and sense of fatigue especially in the latter part of the day.

2. Mental depression and loss of power of concentration

3. Susceptibility to infections.

4. Secondary anemias without apparent cause.

5. Changes in the skin, especially increased sensitiveness to cold, formation of pads, tenderness upon pressure, and, less often, dryness or loss of hair.

6. Unexplained menstrual disorders.

7. Any of the symptoms associated with myxedema may appear singly or in groups but the above symptoms are most common in the early cases. No one sign is infallible, and the therapeutic test sometimes must be employed.

Treatment of Hypothyroidism.— Thyroid extract or thyroxin forms only a part of the treatment. It is needless to say that all possible causative factors should be corrected. Definitely infectious foci should be removed; the proper diet should be prescribed to build up the malnutrition (often visceroptosis) patients and the food should contain sufficient iodin and vitamine principles. Thyroid extract often acts as a stimulant to the appetite, and to the glandular and muscular activities in this type of patient. Many of the cases showing vasomotor instability react to very small doses of thyroid principle.

Postinfective states have been studied in a separate group of cases. Following acute rheumatic fever, tonsillitis, influenza, and other infections, the rate is very often low, the muscles flabby and cellular activity lowered. Many of the symptoms disappear and convalescence apparently is shortened by thyroid stimulation. Whether these cases were subthyroid or normal before their infection, was not determined. A few cases of postinfluenzal melancholia were improved by thyroid feeding. We have had no opportunity to study women in the puerperal state. In the above cases possibly the same results may have wholly or partially been obtained by various "tonics" especially iodin. The older clinicians used iodin in some form very frequently as an "alterative" and the later metabolic studies are showing the accuracy of their clinical observations.

Cretinism and myxedema should be treated continuously with thyroid extract. The most accurate method to determine when the optimum effect has been obtained is by allowing the basal metabolic rate to determine the dosage. The first case of myxedema reported by Murray in 1891 recently died of heart disease at 74 years, having taken thyroid extract since 46 years of age.

Thyroid Therapy.— Many conditions have been attributed to minor thyroid deficiency where the signs and results did not warrant such conclusions. This error has partly arisen from the "therapeutic test." Basal metabolic curves will give truer information, but all conclusions must be guarded. Thyroid extract is a powerful agent "to fan up the fires when they are smoldering," until the body has a fresh chance. A few of the conditions which may be helped by thyroid therapy are the following:—

1. Lowered metabolism with atonicity of muscles, striated and non-striated, producing a multitude of indefinite symptoms. Subnormal temperature is not constant in these cases.

2. Trophic condition of the skin, hair, nails, and teeth. There is no evidence to prove that any skin diseases are primarily due to subthyroidism. Subthyroid cases, upon contracting skin diseases may improve more rapidly if the subthyroid state is corrected.

3. Secondary anemia and occasionally hemorrhagic states.

4. Low blood pressure and low pulse pressure. Occasionally high blood pressure occurs in hypothyroid states and will respond nicely to iodines or thyroid extract. The viscosity of the blood is said to be increased in subthyroid states and iodin is supposed to decrease viscosity.

5. Heart disease. In myxedema the heart action is often slow and feeble, the heart is enlarged to the right and to left, and the electrocardiogram shows signs of myocardial disease. The same may be true in minor cases. We have repeatedly noted patients who clinically and by electrocardiograms showed evidence of serious myocardial degeneration, show rapid gains and improvement of the electrocardiogram, with thyroid feeding, even after removal of focal infection, treatment of toxemias, and other procedures directed toward treatment of the heart muscle had already failed; and then again seen relapses when the thyroid therapy was discontinued.

6. Susceptibility to respiratory infections.

7. Gastrointestinal. Suppression of the secretions, atony,

constipation and intestinal autointoxication may be helped. Cases of achylia or hypoacidity are common and may improve with the general condition of the patient.

8. Albuminuria and occasionally casts.

9. Enuresis in children is sometimes helped by thyroid thereapy.

10. Menorrhagia without other cause.

11. Early sterility, especially with premature menopause are said to be thyroidal in origin. We have had several rates which were low, but no definite improvement after thyroid extract, except in the occasional case.

12. Eye infections (and by one observer, cataracts in dogs) are common in subthyroid animals. In man, Keratitis punctata and slowly healing corneal ulcers are said sometimes to heal more quickly.

13. Tinnitus and deafness due to subthyroidism.

14. Retardation of mental processes.

15. Irritability of temper.

16. Mental depression. There is no evidence that various nervous diseases and many psychoses are directly due to thyroid hypofunction. If such occur in a subthyroid patient, improvement may be noted.

17. Developmental abnormalities.

18. Pregnancy. Hypothyroidism may lengthen pregnancy, and foetal athyroidism or subthyroidism may result.

19. Chronic arthritis is occasionally helped. This condition must be differentiated from myxedematous infiltration about the joints.

Much conflicting evidence occurs in the literature, but the above outline seems to be warranted from a review of the literature and clinical observations. Pathology does not offer much help. Only gross anatomical changes such as atrophy and sclerosis can be observed. Degenerations and inflammations occur in the thyroid similar to other glandular tissue in the body but minor hypothyroid states do not as a rule show gross pathological changes. The clinician must determine when abnormal physiology exists.

Dosage of Thyroid.— Thyroid dosage must be controlled and the basal metabolic rate should not be allowed to go above normal. Physiological hypothyroid cases are often very sensitive to small doses. "Thyroxin" has a more constant potency, but is not necessary. The thyroid extract on the market is usually active, but is variable. A large number of tablets may be prescribed and the dosage determined for the patient. After a few months experience the patients very often can determine what their optimum dosage is by their sensations when the basal rate is within normal limits. When once the optimum amount of "thyroxin" is present in the body, small doses will in many cases maintain the desired effect, but in some patients the principle disappears (or its action) so that relatively large doses are necessary. One grain of the usual extract (we have used Armour's and Parke-Davis and Co.) per day is often sufficient in the minor cases. Some deterioration of the extract occurs when standing and exposed to the air.

What are the Results of Thyroid Therapy.— Many of the most grateful patients are those who have been helped. They have been treated for first one symptom and then another, or not treated at all because they are "neurasthenic." The results sometimes are disappointing, but the attempt is always justifiable. Patients with normal cellular activity are better candidates for good health than those with abnormal, but the pathological changes in the body are sometimes so permanent that nothing will do much good. All other methods for improving the patients' health should be employed, such as hygienic, dietary and corrective; thyroid principle is only an additional, although a very important, aid.

CHAPTER 23.

HYPOTHYROIDISM—THERAPY BY THYROID FEEDING[1]

By N. W. Janney, M.D.

Need for Precise Diagnostic Measure.— The results of a comparative study of the clinical and laboratory data for determining thyroid deficiency are reported herewith. There is very little difficulty in recognizing the average well developed case of myxedema or cretinism, but our observations show that cases of mild thyroid deficiency are probably more numerous than has previously been supposed; also that some will remain unrecognized unless special methods are used in diagnosis and control of treatment.

Examination of the thyroid may be quite misleading. Twenty-five per cent. of our cases exhibited thyroid glands normal to physical examination. It must likewise be remembered that involution of the thyroid takes place as age advances. A small thyroid in an elderly individual is *per se* no evidence of myxedema, unless the gland be scarcely palpable, which should arouse suspicion. Family history suggestive of thyroid disease, fat padding, marked frailty and brittleness of the nails, growth anomalies, tho less frequent, are, when present, of diagnostic importance. Sufficient attention is not always given to examination of the hair and nails, which are very often anomalous in thyroid disease. Distrophies of hair and nails are nearly always present in myxedema, thus bespeaking their relative importance.

Mental symptoms, as a result of latent hypothyroidism, are more common than usually accepted by the neurologist or internist. Very few hypothyroid cases show, if carefully observed, a normal mentality. We look too often for mental lassitude, forgetting that symptoms of mental irritability are also very frequently met with. Sometimes the picture is only that of neurasthenia. It may, however, go on to insanity. In one of

[1] Editor's abstract, N. W. Janney, M.D., and H. E. Henderson, M.D., "Concerning the Diagonsis and Treatment of Hypothyroidism," Archiv. Int. Med., **26**:297-318, Sept. 1920. Approved by Dr. Janney.

our thyroid families, one individual had dementia praecox, another periodic insanity. Such cases may not be on a thyroid basis, but only accompanying degenerative phenomena. Simple failure of memory and the power of concentration are frequently met. A very interesting thyroid family of 62 members has recently been reported by Barrett[2], marked anomalies of the hair and nails being present in many members, together with mental conditions and other signs of degeneration.

In another paper[3], I have emphasized the great value of basal metabolic rate determinations in diagnosis and treatment of hypothyroidism. The differentiation of cases of latent hypothyroidism from neurasthenia, chronic intestinal toxemia, and other debilitated states and conditions is materially assisted by this accurate physical means.

Pathogenesis of Hypothyroidism.— The entire picture of hypothyroidism is that of impairment of tissue growth, regeneration and consequent degeneration due to hormone hunger. It may, indeed, be possible that the great depression of basal metabolism observed in cretinism is partly, at least, of compensatory nature, energy being spared and all metabolic processes being inhibited on account of the inability to adequately utilize fuel and replacement materials. That such an explanation may apply seems likely from the results of basal metabolism determinations in inanition, in which the rates are quite as low as those of the most marked cases of hypothyroidism which have been recorded. All of these varying factors can be understood and correlated with the aid of acceptance of the view that the thyroid gland controls the metabolic processes, anabolic and catabolic, necessary for the required replacement and repair of the organism's cells, together with the production of heat and energy.

General Aspects of Metabolism in Hypothyroidism.— There still remains considerable confusion with regard to modern conceptions of thyroid function. This, to a great extent, has been due to the antithesis between hypothyroid and the so-called hyperthyroid symptoms, as originally drawn by Kocher. . . . Study of the metabolism of hypothyroidism is, however, a greater aid to a clearer conception of thyroid function than the perplexing

[2] Barrett, A. M.: Arch. Neurol. and Psychiat. **2**:628, 1919.

[3] Janney, N. W.: "Hypothyroidism." Barker's New System of Endocrinology and Metabolism.

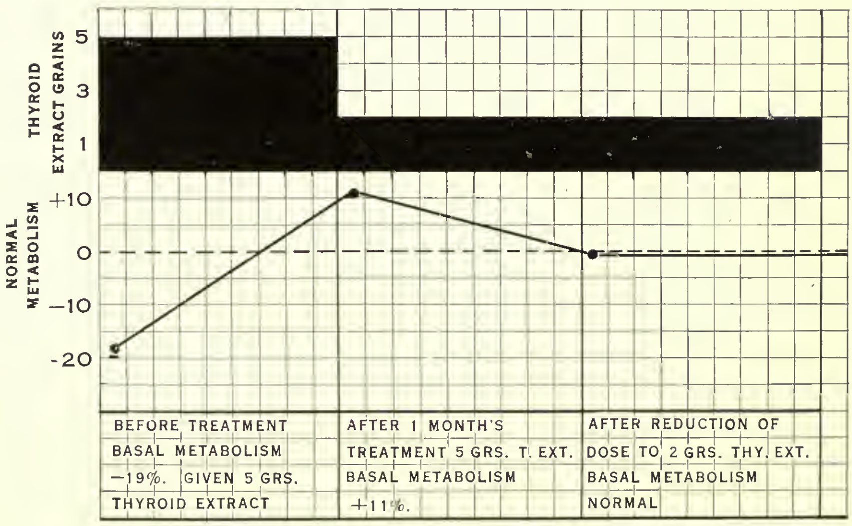
picture of thyrotoxicosis. Since Magnus-Levy's discovery of the decreased metabolic rate exhibited by cretins and myxedematous individuals, little experimental data had been added for a number of years. A reinvestigation of this subject was therefore undertaken in 1915 by one of us (N. W. J.) and his co-workers. This has been continued recently in our Santa Barbara Clinic.

Since the decreased basal metabolic rate of cretins was accounted for by Magnus-Levy and others as being caused by defective food absorption due primarily to alimentary tract sluggishness, exact feeding experiments[4] were undertaken which demonstrated that absorption of food from the intestines of athyroid animals was just as active as in normal animals. This led to further work on cretins, bringing out the fact that thyroid deficient patients failed to absorb as much nutritive material from the intestinal tract as normals, not because the alimentary function was necessarily deficient, but because such subthyroid individuals could not utilize digestive products in the normal manner, whether for fuel, tissue repair, or replacement purposes, *after* this food was assimilated by the intestinal tract. As was clearly demonstrated in prolonged metabolic experiments, when thyroid extract or thyroxin was administered in proper doses to these cretins, there ensued increased intestinal absorption accompanied by and probably required by increased ability to retain nutritive substances in the body and build them into new tissue. These data were obtained by following the nitrogen metabolism. With the demonstration that large amounts, even 100 per cent. more than previously, of nitrogen were retained on proper thyroid dosage, good, if indirect, evidence was secured that the thyroid synthetically controls the growth, probably also the constructive repair and replacement of tissue. The anabolic function of the thyroid gland on metabolism was thus experimentally demonstrated. Hitherto the thyroid was supposed to exert its effect on metabolism solely thru the stimulation of catabolic processes as shown by increased nitrogen loss following the ingestion of thyroid material. Further experiments were therefore carried out demonstrating that the loss of nitrogen in this latter instance is a toxic loss, due to over-great thyroid dosage.

Cases of Decreased Metabolism.— Variations in the metabolic rate are not necessarily due to thyroid disease. Thus we have

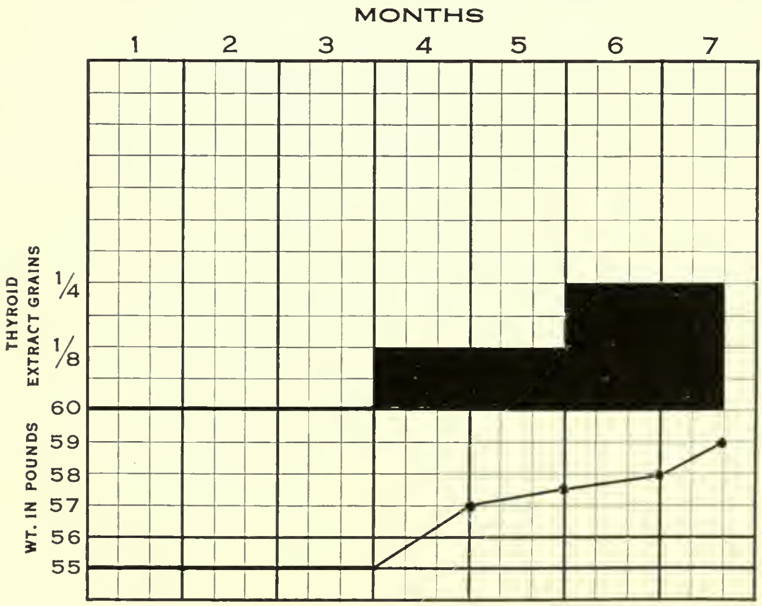
[4] Janney, N. W., and Isaacson, V. I.: Arch. Int. Med. **22**: 160, Aug. 1918.

observed rates of −15 per cent. to −30 per cent. in hypopituitarism. Depression of the metabolic rate from −20 per cent. to −40 per cent. is usually clearly indicative of thyroid deficiency. However, it must be remembered that patients in lowered states of nutrition may show greatly depress metabolic rates. Thus among diabetics without thyroid disease, we have observed rates as low as −35 per cent. The metabolic rate may also fail to serve as an exact criterion in early cases of hyperthyroidism, and even exophthalmic goiter, altho in the vast majority of cases, it is a great aid to the appreciation of the severity of the case as well as to therapy. Thus can be quoted a case of exophthalmic goiter recently observed by us showing thyroid hypertrophy, tremor of fingers and tongue, sympathicotonia, moist palms and soles, nervousness and excitability, exophthalmos, Stellwag's sign, the glistening eyeball, rapid pulse on slight provocation, loss of weight and strength, indeed, all the symptoms necessary for a diagnosis, yet the basal metabolism was 5 per cent. below normal. Sound clinical judgment should never be unduly influenced by laboratory methods.



Treatment of Hypothyroidism controlled by basal metabolism determinations.

Treatment of Hypothyroidism.— It has been our custom for the past year to control the treatment of cases of hypothyroidism by basal metabolism studies. With judicious thyroid treatment, it is surprising with what rapidity the basal metabolic rate rises, accompanied with prompt improvement of all clinical symptoms. In most cases there is excellent parallelism between the clinical course and the basal metabolic rate. Frequently a change in the metabolic rate will give, even before the clinical symptoms, a clear indication for change in dosage. This is, of course, a great advantage in treatment, as the personal factor of clinical judgment can be balanced by an exact physical method. Frequently, too, necessary variations in dosage can be controlled very accurately by metabolic rate determinations. We fear, however, that there will develop a tendency in the profession to put too great confidence in a normal metabolic rate. We have observed several cases of hypothyroidism in which thyroid medication caused a permanent return to the normal rate in short order, but clinical improvement, even after months of treatment, was not very satisfactory. The patients remained over-weight, mentality



Resumption of growth in latent hypothyroidism of childhood with thyroid treatment.

was only partly improved, pulse and temperature subnormal. One must, of course, be mindful that the brilliant results of thyroid treatment in young children cannot always be duplicated in adult cases of many years' standing, where skeletal and other organic changes must be regarded as permanent. Moreover, maximal improvement may require months or even years.

An interesting and discouraging group of cases in regard to therapy are the dysthyroid cases. In these borderline cases, as evidence accumulates, the basal metabolic rate will probably prove very helpful in indicating proper therapy. There is present a confusing complex of "hyper" and "hypo" symptoms, with basal metabolic rates which may be slightly above, below normal, or exactly at the normal level, due regard being given for the limits of error of the method. These cases showing decreased metabolic rates can properly be regarded as preponderantly hypothyroid and given thyroid treatment with expectancy of some improvement. For those showing normal or slightly increased rates, little can be done. A thyroidectomy would incur the risk of subsequent myxedema. Fortunately many of these cases are nonprogressive, some, indeed, being so little inconvenienced by their symptoms that their medical condition is only accidentally discovered.

Now that the thyroid hormone has been duly discovered, its chemical formula and characteristics, also physiologic effect, well established by the splendid researches of E. C. Kendall, it is advisable to use this preparation to the exclusion of all others depending more or less uncertainly on their thyroid hormone content. In 1917, Kendall presented us with an amount of thyroxin for metabolism study at the Montefiore Hospital, New York. Further experience has been gained during the past year, when it has been in routine use. In all ways can we corroborate the findings of the Mayo Clinic as to the physiologic and clinical effect of thyroxin.

Experiments have illustrated that the inability of young hypothyroid individuals to properly utilize their food for fuel and growth has been promptly overcome thru thyroid treatment, as shown in growth chart on preceding page.

Effect upon Appetite.— Thyroid therapy leads to stimulation of appetite, as more food can be assimilated for fuel and tissue construction purposes, increased absorption from alimentary tract, the increased combustion and synthetic utilization of the digestive products, as shown by the rise in basal metabolism and the increase in normal elimination of the purins, as their proper replacement and synthesis in the body is now possible; disappearance of creatin, as a sign of cessation of abnormal tissue breakdown. Regeneration thus takes the place of degeneration of tissues, growth and development return to normal.

Summary and Conclusions.— Latent hypothyroidism is more frequent than generally supposed, as among eighteen consecutive thyroid cases, it was present in twelve, four cases being dysthyroidism and only one presenting classical myxedematous symptoms. Analysis of clinical data shows the following to be present in more than 50 per cent. of our series: history of obesity, particularly in early life, mental symptoms, marked liability to contract infections, hair anomalies, dry, harsh skin with pigmentation and atrophy, cold extremities and cold skin generally, obesity, decreased size of thyroid, subnormal temperature, pulse and respiration. Of all this data, lowered temperature, pulse and respiration occur most frequently, being found in 81 per cent. of our cases. Frequently but few symptoms may be present, diagnosis being impossible without laboratory methods. In the case of children with obscure symptoms, parents should be examined. Attention is called to the diagnostic value of lymphocytosis and mononucleosis in obscure thyroid cases.

The basal metabolic rate is of great value in diagnosis and treatment of hypothyroidism, but cannot be considered an absolute criterion.

Treatment of hypothyroidism is best carried out with Kendall's thyroxin and controlled by estimation of the basal metabolic rate.

CHAPTER 24.

THE BASAL METABOLISM IN FEVER*

By Eugene F. Du Bois, M. D.

Questions Raised by Clinicians.— The clinician has several definite and practical questions to ask regarding the basal metabolism in fever. He wishes to know whether he can calculate the total metabolism of a patient with a given degree of temperature in order to have a rational basis for the fever dietary. It is important for him to know whether there is anything abnormal in the metabolism of proteins, fats, carbohydrates and water. Being interested in the whole subject of fever, he desires information regarding the relative importance of the various factors which increase the metabolism in hyperthermia.

Summary of Available Data.— The answers to the questions must be sought in the voluminous literature of the last thirty years. We have at our disposal a large number of experiments on animals with fever produced by lesions of the central nervous system, by drugs and by artificial infections. These have been well reviewed by Richter,[1] and more recently by Barbour,[2] but they do not give us much help in our problems with man. We have a few experiments on men warmed artificially by hot baths, but in these the effect of the external heat outweighs the fever. We have a large number of experiments on fever patients made by the Zuntz-Geppert apparatus, Benedict apparatus and similar machines which measure the heat production by means of the method of indirect calorimetry. These have given us much information and have laid the foundation of our present knowl-

* Copy of article in Jour. Am. Med. Ass., **77**; 352-357, July, 1921. Paragraph headings by Editor.

From the Russell Sage Institute of Pathology in affiliation with the Second Medical Division of Bellevue Hospital and from the Department of Medicine of Cornell University Medical College.

[1] Richter, P. F.: Fieber, in Oppenheimer's Handbuch der Biochemie.

[2] Barbour, H. S.: The Heat-Regulating Mechanism of the Body, — Physiol. Rev. **1**: 295, 1921.

edge of the metabolism in fever. They have certain disadvantages since the subjects are exposed to different environmental conditions and are more or less disturbed by the application of mouthpieces or masks.

Direct Calorimetry.— The discussion in this paper will be limited almost entirely to the groups of fever patients studied in the respiration calorimeter of the Russell Sage Institute of Pathology in Bellevue Hospital, New York, between the years of 1913 and 1920. Patients and normal controls have been exposed to uniform conditions of environmental temperature and humidity. They have lain almost motionless on a comfortable bed in a quiet respiration chamber for periods of from two to four hours, and in some instances all night. The temperature has been read every four minutes by means of an electrical thermometer which lies about 10 cm. in the rectum. The heat production has been measured by the chemical methods of indirect calorimetry and by the physical methods of direct calorimetry which determine the exact heat loss by radiation and conduction and by the vaporization of water. Incidentally, we may note that the close agreement of these two methods proves that the law of the conservation of energy holds good in fever patients.

The published work consists of studies in typhoid fever by Coleman and Du Bois,[3] in malaria by Barr and Du Bois,[4] and in tuberculosis by McCann and Barr.[5] The unpublished work here presented consists of studies made by Coleman, Cecil, Barr and Du Bois in erysipelas,[6] arthritis[7] and the fever produced by intravenous injections of protein.[8]

Basis of Comparison.— Comparisons with the normal were made according to the usual method of the Sage investigators,

[3] Coleman, W. and Du Bois, E. F.: Clinical Calorimetry, Seventh Paper, Calorimetric Observations on the Metabolism of Typhoid Patients With and Without Food, — Arch. Int. Med. 15: 887 May 1915.

[4] Barr, D. P., and Du Bois, E. F.: Clinical Calorimetry, Twenty-Eighth Paper, The Metabolism in Malarial Fever. — Arch. Int. Med. 21: May, 1918.

[5] McCann, W. S., and Barr, D. P.: Clinical Calorimetry, Twenty-Ninth Paper, The Metabolism in Tuberculosis, — Arch. Int. Med. 26: 663 Dec. 1920.

[6] Coleman, W. Barr, D. P., and Du Bois, E. F.: Clinical Calorimetry, Thirty-Second Paper, The Metabolism in Facial Erysipelas, to be published.

[7] Barr, D. P.; Cecil, R. L., and Du Bois, E. F.: Clinical Calorimetry, Thirtieth Paper, Observations on the Metabolism in Arthritis, to be published.

who consider that the normal metabolism for a given age and sex is proportional to the surface area.[9] Practically all of the

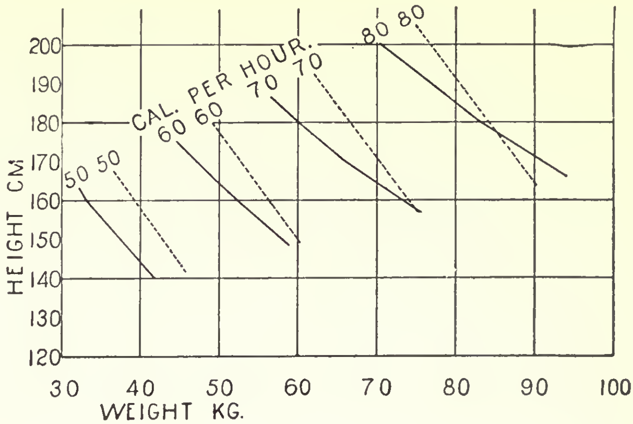


Chart 1.—A comparison of the normal standards for men 30 years old. The solid curved lines give the calories per hour according to the surface area chart and standards of Aub and Du Bois. The dotted lines represent the figures according to the Harris-Benedict multiple prediction tables. For instance, a man 30 years old, 180 cm. tall and 60 kg. in weight would have a predicted normal basal metabolism of 70 calories per hour according to the surface area curves, and about 67 calories per hour by the other method. The results according to the Harris-Benedict formula are lower, but the two sets of lines are almost parallel for this age group.

subjects studied were between 20 and 40 years old, and the standard used for this age was 39.5 calories per square meter per hour.[10] If we express the matter graphically on a chart (Chart 1), we can show the curves for the predicted metabolism of normal individuals of different heights and weights. If metabolism were proportional to height, these lines would be horizontal;

[8] Cecil, R. L.; Barr, D. P., and Du Bois, E. F.: Clinical Calorimetry, Thirty-First Paper, The Effect of the Injection of Foreign Protein on Metabolism to be published.

[9] Du Bois, D., and Du Bois, E. F.: Clinical Calorimetry, Tenth Paper, A Formula to Estimate the Surface Area if Height and Weight be known, — Arch. Int. Med. **19**: 863 June, 1916.

[10] Aub, J. C., and Du Bois, E. F.: Clinical Calorimetry, Nineteenth Paper, The Basal Metabolism of Old Men, — Arch. Int. Med. **17**: 823 May 1917.

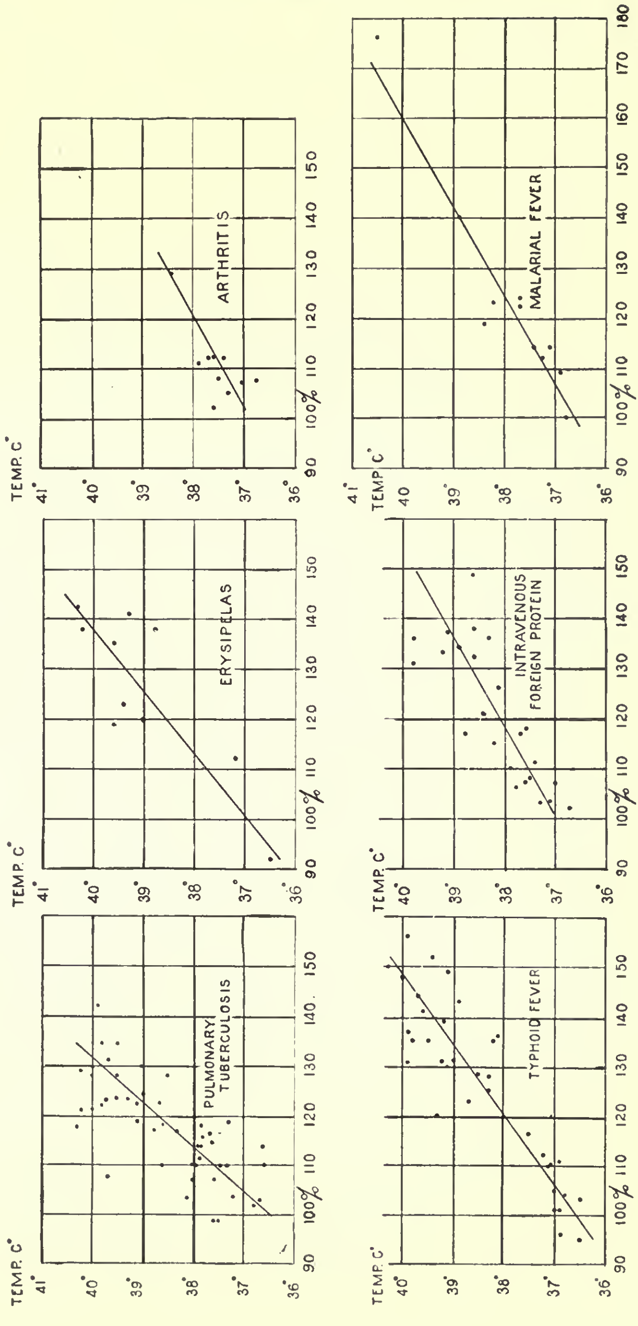
if proportional to weight, they would be vertical. If proportional to surface area, they would have the slant shown in the curved solid lines of the chart, and our results do agree with these curved lines. A purely statistical study of the normal basal metabolism by Harris and Benedict[11] has resulted in a height-weight-age formula. With a little calculation we can show their results for men 30 years old on this chart. It is significant that the dotted lines for the Harris-Benedict formula are parallel to the surface area curves.

The studies of large groups of normal controls show that about 90 per cent. of normal men come within 10 per cent. of this standard; but a few who are apparently normal may show figures as much as 15 per cent. above or below.

Can we predict the metabolism as closely as this for any specified degree of fever?

Discussion of Results Obtained.— Chart 2 shows the results in all the fevers studied in the calorimeter, expressed by the method used by McCann and Barr in tuberculosis. The ordinates show the rectal temperature in degrees Centigrade. The abscissas show the level of the metabolism in percentage of the average normal. The line 90 means 10 per cent. below the average; 150 means 50 per cent. above the average. Each dot denotes an experiment of from one to three hours at a given temperature level. The normal temperatures were obtained in afebrile periods or in the first eight days of convalescence The diagonals are sketched to represent the direction of the swarms of dots. It will be seen that in tuberculosis the diagonal crosses the 40°C. line at a level of about 32 per cent. above the normal. In many of these patients there was enough undernutrition to account for a certain diminution in metabolism. In erysipelas the metabolism is a little higher for the same temperature. In typhoid fever, the line crosses the 40-degree level at 48 per cent. above the normal metabolism. In malaria and the fever following the intravenous injection of foreign protein, the metabolism is slightly higher. Of course, it is necessary to leave out the shivering periods in these two conditions. It is possible that some of the results in the high temperature following the chill are slightly affected by the previous severe muscular exercise.

[11] Harris, J. A., and Benedict, F. G.: A Biometric Study of Basal Metabolism in Man, Publication 279, Carnegie Institution of Washington, 1919.


ARTHRITIS
ERYSIPELAS
PULMONARY TUBERCULOSIS
MALARIAL FEVER
INTRAVENOUS FOREIGN PROTEIN
TYPHOID FEVER
TEMP. C°
41° 40° 39° 38° 37° 36°
90 100% 110 120 130 140 150 160 170 180

Protein Metabolism.— Most of the patients whose metabolism is very high for the degree of temperature were typhoid or malaria patients with a high level of protein metabolism. Most of those with low basal metabolism were tuberculous patients with low protein metabolism. We know that protein increases the metabolism through its specific dynamic action, and this may explain the difference between the groups of patients. The ingestion of a large protein meal does not increase the heat production in typhoid fever, in which the protein metabolism is already high, but it does cause a striking increase in tuberculosis in which the protein metabolism is at a much lower level. Although the increased protein metabolism seems to be a factor of some mportance, we believe that it is outweighed by another and impler factor.

Normal Metabolism for Given Temperature— We note particularly the similarity betwen fevers of greatly different origins, such as typhoid and erysipelas, malaria and intravenous injections. We are impressed by the importance of the nonspecific element in fevers. This is even more striking, if we group all the heterogeneous fevers in one chart (Chart 3). The continued diagonal line is here drawn from statistical calculations, and the dotted lines are placed to represent divergences of 10 per cent. from this average. Out of the total of 137 experiments in various fevers, 82 per cent. come within 10 per cent. of the average. In other words, the percentage variations in the metabolism for a given temperature are scarcely greater than in a similar group of normal individuals.

Van't Hoff Law.— This surprising uniformity of results suggests at once that we are dealing with the law of physical chemistry enunciated by van't Hoff.[12] For ordinary temperatures the van't Hoff law can be thus expressed: "With a rise in temperature of 10 degrees Centigrade, the velocity of chemical reactions increases between two and three times." In other words, the temperature coefficient is usually between 2 and 3. This means an increase of from 30 to 60 per cent. for the 3 degree rise from 37 to 40 C. Practically all of the fever experiments are within these limits. and the average line shows a temperature coefficient of 2.3.

[12] Van't Hoff, J. H.: Studies in Chemical Dynamics, Revised by E. Cohen, Translated by T. Ewan, Easton, Pa., Chemical Publishing Company, 1896.

Van't Hoff and Kanitz[13] give the temperature coefficients which show the rate of increase in a number of chemical reactions

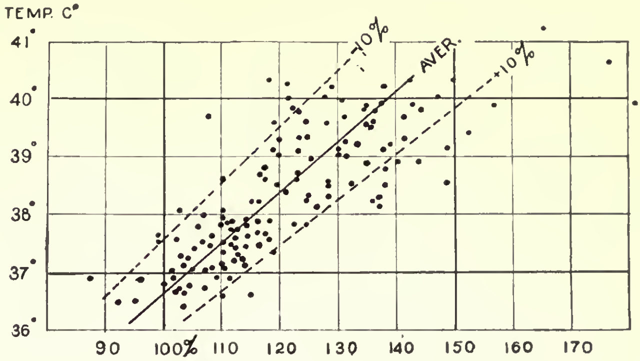


Chart 3.—Results in six different fevers grouped in one chart. The continued line shows the average and the dotted lines are drawn to represent metabolism 10 per cent. above and 10 per cent. below the average.

with an equal rise in temparature. If we plot these in exactly the style of the fever patients (Chart 4) we note that the lines

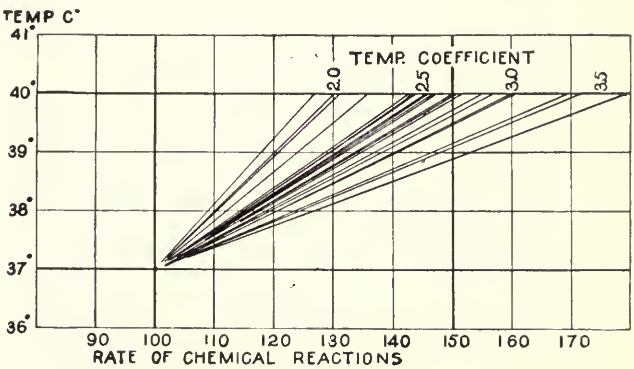


Chart 4.—The lines in this chart represent a number of typical chemical reactions taken from van't Hoff and Kanitz. The slant of the lines shows the increase in the rate of the reactions as the temperature is raised. Note that the lines correspond closely to those which represent the total oxidations in the human body.

[13] Kanitz, A.: Temperatur und Lebensvorgänge in Biochemie in Einzeldarstellungen, Vol. 1, Berlin, Gebrüder Borntraeger, 1915.

have approximately the same slope. In other words, the reactions in a fever patient respond to a rise in temperature in a manner which resembles closely the chemical reactions in a test tube suspended in a water bath.

There is a tremendous gap between the simple reactions in the test tube and the complex oxidations in the diseased human body, and we should hesitate to compare them were it not for the large number of biologic reactions which show temperature coefficients between 2 and 3. Van't Hoff calls attention to the rate of carbon dioxid elimination in plants, which shows a coefficient of 2.5. Kanitz[1] gives a long list of similar coefficients for plant respiration, rate of isolated hearts, contraction of smooth muscle and the metabolism in cold blooded animals.

Malarial Chill.—We have seen that the gross results in different fevers are strikingly similar. It is interesting to note the similarity in the details of the mechanism of the rise and fall of temperature in the chills of malaria and those which follow the

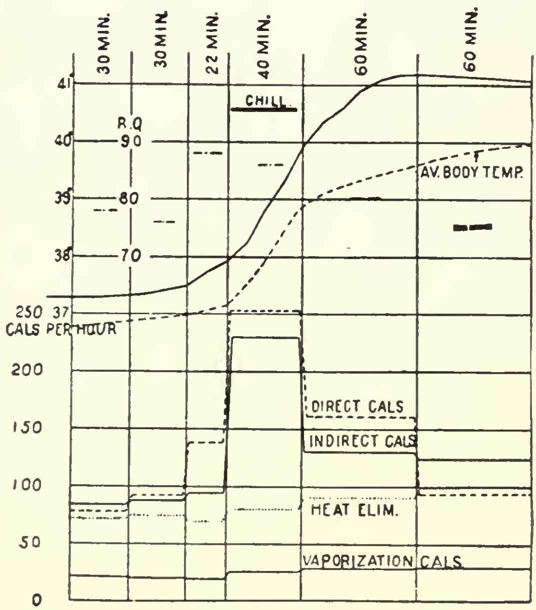


Chart 5.—Calorimeter results during a malarial paroxysm. The upper continued curve shows the rectal temperature.

intravenous injection of foreign protein. The first curve (Chart 5) shows the results obtained in a malaria patient by Dr. David P. Barr and myself. Before the chill the metabolism and temperature were normal. In the period of the thirty-four minute chill there was terrific shivering, and as a result the heat production rose to 216 per cent. above normal. After the chill the metabolism was increased by the hyperthermia, and then fell gradually as the temperature became lower. The chill was accompanied by no change in the heat elimination. The old idea that the rise in temperature is largely caused by a decreased elimination has been proved false. The rise is due to the increased heat production, and this is caused in part by shivering and in part by some chemical regulation, the nature of which is still in doubt.

After the temperature has reached its zenith, the elimination must, of course, exceed the heat production.

Errors in Measurement.— The curve of the rectal temperature does not always parallel the curve for the changes in the average body temperature. We shall never know the exact level of the average body temperature, because we cannot place ther-

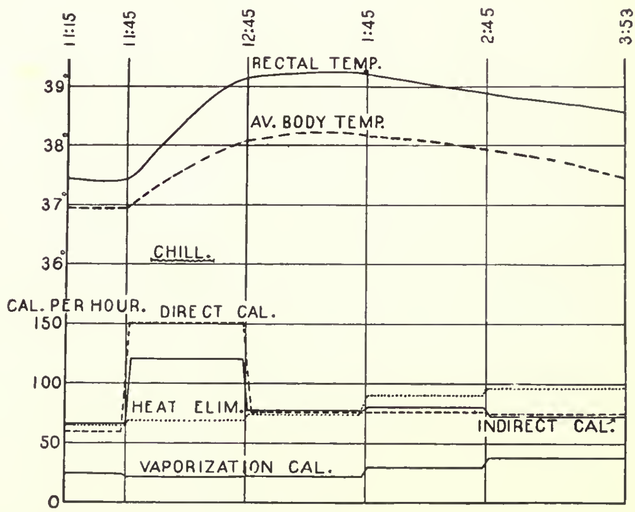


Chart 6.—Calorimeter results following the intravenous injection of 35 million dead typhoid bacilli. The percentage rise in metabolism does not appear so great because the chill occupied only a portion of the period between 11:45 and 12:45.

mometers all over the extremities and in the viscera; but if we know the differences between heat production and heat elimination, we can calculate how many calories have been stored in or lost from the body, using the method devised by Barr.[4] If we start the average temperature curve half a degree below that of the rectal temperature, we can then follow its changes. Apparently the region whose temperature is measured by a thermometer deep in the rectum shows a more rapid rise than the whole body, with its large mass of tissue near the surface and in the extremities.

The curve of the arthritic patient who was given an intravenous dose of 35 million dead typhoid bacilli is almost identical with that of the malaria patient (Chart 6).

A Study of the Respiratory Quotient.— A study of the respiratory quotients in various fevers indicates that there are no significant changes in the metabolism of fat and carbohydrate. Protein metabolism is high in fevers, and the protein minimum or "wear and tear quota" cannot be reduced to the normal level. This increase seems to be proportional to the toxemia, since it is excessive in patients seriously ill with typhoid and erysipelas, and comparatively insignificant in chronic tuberculous patients with the same degree of fever.

Water Metabolism of Fever Patients.— Balcar, Sansum and Woodyatt have produced excessive fever in dogs by depleting the water reserves of the body, and they infer[14] that an abnormal water metabolism may be the cause of fever in man. If this were the case, we should expect to find striking abnormalities in the total or percentage loss of heat through vaporization in febrile patients. A careful scrutiny of the calorimeter results shows no such phenomenon. The water metabolism of fever patients corresponds closely with that of patients with an equal percentage rise in metabolism caused by hyperthyroidism.

Conclusions.— Let us now answer the original questions. We can say that it is possible to estimate the basal metabolism of a patient by calculating his normal according to surface area standards. To this we should add about 13 per cent. for each degree Centigrade above the normal temperature (7.2 per cent. for each degree Fahrenheit). This should be increased by 10 per cent. in the case of toxic patients with great destruction of

[14] Balcar, J. O.; Sansum, W. D., and Woodyatt, R. T.: Fever and the Water Reserve of the Body, Arch. Int. Med. **24:** 116 July, 1919.

body protein, and by approximately 10 per cent. in all other febrile patients who are receiving much food. A further allowance of from 10 to 30 per cent. for muscular activity may be necessary if the patients are restless.

It is interesting to note that our practical calculations in the clinic are based on the law of the conservation of energy, on the surface area law of Rubner, on the laws of the specific dynamic action of foods as formulated by Rubner and Lusk,[15] and on the temperature law of van't Hoff.

[15] Lusk, Graham: Science of Nutrition, Philadelphia, W. B. Saunders Company 1919.

CHAPTER 25.

OBSERVATIONS ON THE BASAL METABOLISM ESTIMATES IN THE GOITER CLINIC OF THE UNIVERSITY HOSPITAL.[1]

By Charles H. Frazier, M. D.

Basal Metabolism as a Diagnostic Measure.— The metabolic rate is of special value in diagnosis in that it offers a ready means of distinguishing cases of true hyperthyroidism from those cases of neurasthenia, cardiovascular disease or tuberculosis, who present the clinical picture of toxicity and who happen to have a simple adenomatous enlargement of the thyroid. These cases are often sent to the surgeon as a court of last resort. Such cases would naturally not be benefited by any operation and might be made a great deal worse. The metabolic rate enables us to decide for or against operation in cases in which there is little or no perceptible enlargement of the thyroid gland, and in which the only evidence of toxicity is tachycardia.

Basal Metabolism as a Therapeutic Guide.— It has been our practice to take readings on all goiter cases before and after treatment, whether that consist in ligation or thyroidectomy. If the case comes to ligation as the initial step in treatment a second reading is taken either before leaving the hospital or when the patient returns for thyroidectomy several months later. The final reading, after all treatment is over, is usually made within a year from the last operation, when the patient returns for final observation.

Classification of Cases.— For the convenience of study and analysis we have divided our cases into 4 groups, based on the metabolic rate.

Group 1. Basal metabolic rate from 10 to 20%
Group 2. Basal metabolic rate from 20 to 40%
Group 3. Basal metabolic rate from 40 to 60%
Group 4. Basal metabolic rate from 60 and up

[1] Abstracted from article of same title in American Journal of the Medical Sciences, July 1921. Abstract approved by author.

At the same time we have graded our cases according to the symptomatic evidence of toxicity alone. This is done without a knowledge of the metabolic rate. In Group 1 we place the mildest cases, i. e., those with the lowest grade of toxicity; and in Goup 4 the severest cases, i. e., those with the highest grade of toxicity. Groups 2 and 3 are intermediate. We find that there is a certain conformity between the groups graded by the clinical picture and graded by the metabolic rate. In fact, the conformity is sufficient to enable us to say that in the majority of cases we have in the basal metabolic rate a numerical index of the patient's toxicity. This gives us at once a means of classifying our patients, a guide to the treatment and a measure of the improvement under any particular treatment.

Surgery.— In treatment we find that we may be guided by the metabolic rate in the choice of operations. Thus in Groups 1 and 2 we may proceed with a subtotal thyroidectomy at once. In Group 3, in the majority of cases, we first do a bipolar ligation; only occasionally a thyroidectomy as the initial procedure. In Group 4 we never do a thyroidectomy first but choose either unipolar or bipolar ligation.

The Metabolic Rate as a Check on Therapy.— The metabolic rate is also useful in determining the amount of improvement which any course of treatment may have effected. It is interesting to note that after ligation the average reduction is greater than after thyroidectomy. That the two figures cannot be compared, and any deductions drawn, as to the relative value of these two procedures is evident when we consider the type of case which is selected for ligation. Those cases which have a preliminary ligation have the highest metabolic rates. In reducing the metabolic rate it is as tho we were reducing the height of a pyramid; much less effort is expended in taking away the top half, the labor increasing with each successive step. It is easier therefore, to cut down the top half of a high metabolic rate by ligation than to remove the remainder, this more difficult part of the work being accomplished by the thyroidectomy. The reduction in total points, therefore, is less after thyroidectomy than after ligation.

Conclusions.— In conclusion, our experiences at the clinic show that the estimations of basal metabolism are of value in the following cases:

1. **Positive.**— In eliminating those cases which will not be benefited, and might be made worse by operation.
2. **Supplemental.**— In offering confirmatory evidence of the degree of toxicity; and in offering a quantitative rather than a qualitative index for use in diagnosis, prognosis and treatment.
3. **Problematical.**— It may be possible by the metabolic rate to determine how much thyroid tissue may be removed. The reduction of the metabolic rate to points well below that of the normal range (−10 per cent.) should imply that too much secreting substance had been removed. Such cases must be studied clinically for signs of hypothyroidism.

CHAPTER 26

BASAL METABOLISM AS AN INDEX TO SURGICAL TREATMENT[1]

By Frank H. Lahey, M.D.
and
Sara M. Jordan, Ph.D.

The Value of Metabolism Studies.— Basal metabolism as a diagnostic measure, altho subject to error in estimation and interpretation, is probably more constantly reliable than many of our other laboratory measures, both as to its qualitative and quantitative value. It is of the greatest value in hyperthyroidism since that disease is so distinctive in its course and symptoms, and so characteristically a disease of hypermetabolism.

From our experience in metabolism studies in connection with thyroid disease, involving 304 metabolism estimations on 135 patients, it does not seem that active hyperthyroidism exists without an increase in the metabolic rate.

Such a study is of value, further, in determining the presence of secondary hyperthyroidism in those cases of adenoma of the thyroid in which the symptoms of hyperthyroidism are not markedly evident. It used to be a source of considerable surprise to us in the beginning of our thyroid experience, before we were accustomed to employ basal metabolism estimation, to find that many patients upon whom we operated merely to remove an adenoma which was either causing pressure or was unsightly, came back within a few months, having gained in weight, and stating that they felt a marked change in their general health. This we now know to have been an improvement from secondary hyperthyroidism which, when well marked, is — with the exception of exophthalmos — similar in every way to primary hyper-

[1] Editor's abstract, "Basal Metabolism as an Index of Treatment in Diseases of the Thyroid," by Frank H. Lahey, M.D., and Sara Murray Jordan, Ph.D., Boston Med. and Surg. Jour. 184:348-358, April 7, 1921. Approved by Dr. Lahey.

thyroidism, and no more difficult to demonstrate: Its presence, however, in mild or pre-states of clinical hyperthyroidism is not easily demonstrated clinically, but even slight degrees of secondary hyperthyroidism are demonstrable by increases in the rate of metabolic activity.

Metabolism Determinations as an Index to Surgical Treatment. — Metabolism estimation, correlated with the clinical examination, is also of marked value in indicating the ability of a patient to withstand surgical procedures of various magnitudes; for example, in deciding whether the ligation of a single thyroid pole should be employed, whether it would be wise to ligate both thyroid poles, or whether it would be safe to employ partial thyroidectomy as a primary procedure. It is of further value in deciding when to follow the preliminary pole ligation with the partial thyroidectomy. Until recently it has been our custom to ligate the superior thyroid poles and then to send the patient home for eight weeks, at the end of which time the patient returned to the hospital for the complete operation. As the result of our metabolism investigations, we have been finding that in some cases, by waiting eight weeks, we have passed the period of maximum improvement, as indicated by a rise in the metabolic rate from the rate representing the maximum drop after pole ligation. We have, therefore, come to the conclusion that during the intervals between pole ligation and partial thyroidectomy, metabolism estimations should be made every two weeks, and partial thyroidectomy employed as soon as the maximum gain indicated by a drop in metabolism and pulse rate is made.

Necessity for Correlating Clinical Picture with Metabolism Estimations.— We feel that in hyperthyroidism the metabolic rate alone is not a true criterion of the seriousness of a patient's condition, and, considered alone, is unreliable as a guide to the extent of the surgical procedure to be employed. That thyroid toxicity is represented by increased basal metabolic rates, there can be little question. However, we feel very strongly that the level of the basal metabolic rate alone is quite undependable, and in fact often misleading as a means of prognosticating the seriousness of the patient's state and her ability to endure any surgical procedure. We have had surgical experiences with patients showing metabolic rates at both extremes, in which the course and results of the operative procedure have been entirely out of accord with what might have been expected from the metabolic rate.

It is, therefore, evident that it is impossible to make any fixed statement concerning the percentage figures in basal metabolism at which it is safe to perform partial thyroidectomy as a primary procedure. Neither is it possible to state at what level of the basal metabolic rate it is wise to ligate but one pole, nor is it further possible, from basal metabolism estimations alone, to weed out the cases too seriously afflicted to be submitted to any surgical procedure and to be relegated to the less satisfactory and more prolonged methods of treatment not surgical in nature, such as rest and X-ray treatment.

Yet with the previous view clear in our minds, we are willing to make certain approximate groups which we believe, from our experience, work out satisfactorily in a majority of cases.

Partial thyroidectomy may be employed as a primary measure, unpreceded by ligations, in most of the cases showing increases in metabolic rates of not over +35 per cent. In all such cases, however, careful consideration must be given to the apparent degree of toxicity of the disease, as evidenced by the clinical signs, and this consideration must not be biased by the degree of increase in the basal metabolic rate, however moderate it may be. Careful consideration must also be given resulting or associated lesions, such as myocarditis and renal lesions.

Fine judgment, based largely upon an extensive experience as to how similar cases have acted under various surgical procedures, is necessary in deciding between pole ligation and primary partial thyroidectomy in the cases of hyperthyroidism showing increases in basal metabolic rates of between +35 per cent. and +50 per cent. Decision as to the type of operation should be left until the patient is on the operating table and anaesthetized, and should then be made only when based upon the known basal metabolic rate, the pulse rate, its character and rhythm, and with a consideration of the possible degree of post-operative thyroid reaction. When doubt exists even in the slightest degree as to the safety of primary partial thyroidectomy, we ligate.

Most patients showing basal metabolic rates above +50 per cent. are safest when submitted to primary ligation of one or both of the superior thyroid poles. It is our custom in these cases to reserve decision until the patient is anaesthetized (scopolamine, morphia, novocaine + gas oxygen), making use of the same measures as stated above. The decision is then made whether the patient shall be sent back to bed to observe the degree of reaction to the anaesthesia and visit to the operating room, or whether ligation of the poles shall be proceeded with. If the latter procedure is decided upon, one superior pole is rapidly ligated and decision as to whether ligation of the other superior pole is to be carried out is based upon the immediate condition of the patient and how she has endured the ligation of a single pole.

With patients showing metabolic rates of from +75 per cent. up, extreme caution must be exercised in the extent of the surgical treatment. In the doubtful cases, a visit to the operating room and the administration of gas oxygen anaesthesia with no operative procedure gives valuable evidence as to the resulting degree of reaction. In the less doubtful cases, the ligation of a single pole with a wait of ten days to two weeks makes the ligation of the second pole very much more safe for the individual.

Caution in Thyrotoxicosis.— It is our opinion that there is hardly a surgical disease in which caution is as necessary as in the cases of marked thyrotoxicosis. As they approach the higher levels of toxicity as indicated by clinical signs and increases in metabolic rates to a high level, each case should be individualized and no longer looked upon as being a member of a group. After such cases have reached the more intense stages of thyroid intoxication, they no longer conduct themselves by rule. This statement is more or less true of hyperthyroidism as a whole, but is particularly characteristic of the intensely toxic cases. After an extensive experience with thyroid cases, we feel able to prophesy with relative certainty the course and reaction of mild and moderate degrees of thyroid intoxication to various surgical procedures, but have by no means the same degree of assurance regarding the intensely toxic cases. It is because of this unknown capacity for unfavorable reaction on the part of severely toxic cases that extremely cautious advance should be made. First, the degree of reaction to the slight discomfort and apprehension which goes with the estimation of basal metabolism; next the reaction to a visit to the operating room and short gas-oxygen anaesthesia, and finally, based upon this data, the ligation of a single thyroid pole. Having advanced so far, we have accumulated sufficient data upon which to base with reasonable certainty a decision as to the probable outcome with further surgical procedures.

Clinical Complications. — Care must be taken, in thyroid cases, to ascertain the presence of complicating conditions which seriously affect the metabolic rate. For example, diabetes, in our experience, has not been a rare complication of hyperthyroidism (or vice versa, if you choose), and in such a condition care must be taken to ascertain to what diet and to what treatment the patient has been subjected.

Care must also be taken to ascertain possible renal lesions, marked examples of which are said to give increased metabolic rates.

Seemingly simple infections giving but low degrees of temperature reaction must also be eliminated, as fever very promptly results in a marked increase in the metabolic rate.

In thyroid cases, basal metabolism estimation should not be undertaken at a time too close to the period following the performance of the Goetsch or epinephrin test as injections of epinephrin have resulted in our experience in well marked rises in the metabolic rate.

Apprehension, anxiety, and excitation play a considerable part in the production of unreliable data in metabolism estimation, and where even the possibility of such influence occurs the test should be repeated daily until an average is struck or the patient eliminated as a subject from whom a reliable result may not be obtained.

Conclusions.— When all the factors, that are described in the paper, can be eliminated and the basal metabolic rate can be regarded as a true index of thyroid activity, it may be said in conclusion that, in our opinion, in a clinic for diseases of the thyroid, a test of the rate of basal metabolism is an invaluable factor in the data necessary for diagnosis; second, that it aids greatly in prognosis; third, that it probably has its greatest value as an index of the results of treatment in any given case.

CHAPTER 27

A CONSPECTUS OF RECENT ADVANCES IN METABOLISM

For the purpose of presenting some of the new developments in the field of basal metabolism, recent papers by qualified authors have been reviewed. From them, relevant material that has not already been included in this book has been extracted and is presented in summarized form as below:

1. Comparative Normals of Children.
2. Normal Metabolism After a Light Diet.
3. An Aid in Prognosis.
4. Classification of Goiter.
5. Effect of Menstruation.
6. Pregnancy and the Puerperium.
7. Chronic Pulmonary Tuberculosis.
8. Respiration in Tuberculosis.
9. Thyroxin.
10. Pituitary Extract.
11. Dysfunction of the Liver.
12. Myelogenous Leucemia.
13. Kymograf Records.

Comparative Normals of Children.— Blunt[1] made observations on 28 children, chiefly underweight, ranging from 9 per cent. to 27 per cent. but revealing no clear symptoms of hyperthyroidism or other organic disturbances. Three or four determinations of two 10 minute periods were made on the majority of the children, on an apparatus measuring only the oxygen consumption. The calories per square meter of body surface per 24 hours obtained for this series were in every case higher than the standards according to Benedict. Altho there was an excess metabolism as high as 40 per cent. no relation was observed between the percentages metabolism increase and the percentage underweight.

[1] Blunt, Nelson, and Oleson: The Basal Metabolism of Underweight Children — Jour. Bio. Chem. 49:.247-262, Nov., 1921.

Benedict[2] studied 23 children, ranging from 2 to 15 years of age for periods of a few months to 3 or 4 years. A modified respiration chamber was used, in which the carbon dioxid content was determined by weight of the absorbent bottles, and the oxygen content by a meter. The periods of 20 to 30 minutes were repeated as often as was advantageous. The conclusion drawn from this large series of tests is that the metabolism of the child is most dependent upon the body weight, girls manifesting, however, a constantly lower figure.

Klein[3] propounds the belief that extensive determinations upon the same subject are more exhaustive and valuable than 1 or 2 tests upon many children. His figures are, therefore, the report of tests upon only 2 boys. Eight tests of 10 hours each were made in a respiration chamber, cautiously guarded for tightness. The heat exchange was calculated from the oxygen and carbon dioxid content of the expired air. For the metabolism the Lissauer and Meeh formulae are used.

From each of these authors one case has been selected of approximately the same height and weight, and of the same sex, to compare the results:

		Height cm.	*Weight kg.*	*Age*	*Cals per sq. m. per 24 hrs.*
Blunt,	Case John	125.8	23.2	8 y. 1 mo.	1213
Benedict,	Case No. 215	116.5	20.8	8 y. 2½mo.	1165
Klein,	Case Kurt	114.0	22.2	7 y.10 mo.	1079

Case John was 10 per cent. underweight, and determined in the post-absorptive condition. Case No. 215, "somewhat thin" but otherwise normal, was not allowed food before the test. Case Kurt, the normal figure for which is the lowest, was allowed a restricted diet on the day preceding the night of the test, during which it must be remembered that the boy was asleep, which factor alone might account for the lower figure.

Normal Metabolism After a Light Diet.— Recently Baumgart and Steuber conducted experiments in the pneumatic cabinet of the Physiological Institute in Berlin to determine the basal metabolism of 2 boys who were in the fasting state. After their

[2] Benedict and Talbot: Metabolism and Growth from Birth to Puberty — Carnegie Inst., Washington, Pub. No. 302, 1921.

[3] Klein, Muller, and Steuber: Beitrag zur Kenntnis des energetischen Grundumsatzes bei Kindern — Archiv. fur Kinderheilkunde, Stuttgart, Oct. 29, 1921.

painstaking work, they found it to be 100 cals. lower than Rubner's constant for heat production, which decrease they attributed, judging from the R. Q., to the post-absorptive condition of the children.

The authors[3] believed that a more exact figure would be obtained if the subjects were allowed nourishment, preferably liquid, and of a definite amount. As subjects, two 8 year old boys were chosen who had always been in good health, and were well developt in regard to height and weight. All experiments were made at night during sleep, lasting 10 hours, with the following preceding diet:

Breakfast 7:00 A. M.	50 g. rice, 25 g sugar, 50 c.c. milk Total about 350 cals.
Noonday lunch	30 g. sago cooked in water with one broth cube and salt. Total about 126 cals.
Tea at 3:00 P.M.	250 c.c. tea with saccharin.
Tea at 8:00	250 c.c. tea with saccharin.

The experiment began about 9.00 P. M., after the boys had been taken for a walk to insure a good night's sleep. It was rather to the experimenter's amazement that the boys experienced no hunger.

Two reasons are given for performing the experiments on 2 boys at once: First, by one another's company to allay any fears that the closed chamber might arouse. Second, to rule out the personal factor: one of the boys was very phlegmatic; the other, lively.

The tightness of the apparatus was checked by the nitrogen content, at the beginning and end of each experiment. Respiration quotients varied from .78 to .93.

Altho the boys' height and weight were almost identical, 114 and 113 cm., and 22.2 and 21.6 kg., respectively, the individual body surface area was calculated and the average used.

The heat production during rest and sleep by the Meeh formula was 1033.8 cal. per 24 hrs. per sq. m. of body surface; by the Lissauer formula, 1123.9 cals.; and per kilo of body weight, 44.52 calories.

An Aid in Prognosis.— Wilson[4] considers the determination

[4] Wilson, C. M., and D.: The Determination of the Basal Metabolic Rate, and its value in Diseases of the Thyroid Gland. Lancet, Nov. 20, 1920.

of the basal metabolic rate helpful to bring out the value of rest and its limitations, to define the role of drugs, to separate the type of case the X-ray benefits from the larger group in which it is of no avail; and with regard to surgery, to lay down precise rules for our guidance. We know now when nonsurgical measures have done what they can do, when the choice rests between surgery and continued thyroid over-activity. We are told by this means not only under what conditions operation is necessary and beneficial, but also when the appearance of the surgeon is of evil omen. Finally, these measurements enable us to detect the malady, and the relapses of that malady after treatment at a stage when active measures will rapidly restore normal function.

In therapy, basal metabolism determinations mark off toxic from non-toxic goiter, establish or refute suspicions of hypo- or hyper-thyroidism, and furnish a grafic record of the results that follow the treatment of these conditions, so that the selection of the line of treatment becomes less capricious and comes to rest upon exact methods.

Classification of Goiter.— Mayo[5] has presented the manifestations of various types of goiter at the onset of the disease, stressing the basal metabolism test as a diagnostic measure to differentiate particularly between toxic goiter and psychoneurosis.

Mayo mentions first, Basedow goiter, which may remain inactive for from 14 to 20 years with no exophthalmos, but with hyperthyroidism. This is not to be confused with Basedow's disease, the German term for exophthalmic goiter.

In true exophthalmic goiter there is an hypertrophy of the epithelium causing crowding of the vesicles and no retention of secretion. Altho with this type of goiter hyperthyroidism is not manifest until about 43 years of age, Mayo states that he has seen children under 10 with typical symptoms of exophthalmic goiter, such as tremor, tachycardia, nervousness and exophthalmos.

A small hard, symmetric gland, not exophthalmic goiter, may be tuberculous.

All cystic goiters are the result of degeneration following failure of the blood supply of the encapsulated adenoma. The

[5] Mayo, Chas.: The Thyroid. Medical Record, July 30, 1921.

cystic goiter is encapsulated and thus the thyroid is converted into an extra capsule.

Toxic adenoma producing hyperthyroidism appears in the average case at 43 years, and yet the average age at which these patients are operated is 48 years.

Carcinoma of the thyroid rarely produces symptoms early in the course of the disease. If there are irregular, hard nodules in the gland it is probably malignant, especially if the adjacent lymphatics are enlarged. Exploration, with examination of tissue is, however, necessary for diagnosis.

Substernal goiter is more common than was supposed. Sometimes its presence is indicated by the veins on the neck extending down over the chest, showing the obstruction to the venous flow. This type of goiter is frequently well encapsulated and can be easily enucleated, especially if the patient cooperated by a little cough. In order to have the advantage of the cooperation of the patient, operations on goiters of this type should be performed under local anesthesia.

Syphilitic goiter is not very common, and sarcoma is rarer than carcinoma.

Effect of Menstruation.— No significant difference is noted for the pre- and intermenstrual periods of normal women, including a series of 216 observations[6] on 17 women, 14 of them covering 1 or more menstrual cycles, and 1 being observed for 26 almost consecutive days. The authors also note no regular, rhythmic, day by day variation. With a number of subjects a high metabolism day can be found just before or at the beginning of menstruation but so also can a low metabolism day.

That there is no regularity of variation is corroborated by Zuntz, who in 1906, determined the carbon dioxid output and part of the time the oxygen consumption for 2 women for 97 days, almost without a break, including 3 menstrual periods with inter-, pre-, and postmenstrual observations. He noted no variation that he attributed to menstruation.

Wiltshire[7] has recently completed observations on 5 normal women during the menstrual period, with an average of from 25

[6] Blunt, K. and Dye, M.: Basal Metabolism of Normal Women. Jour. Bio. Chem., June, 1921.

[7] Wiltshire, M. O. P.: Some Observations on Basal Metabolism in Menstruation. Lancet, Aug. 20, 1921, 0p. 388.

to 58 tests upon each case, collecting the samples of air by the Douglas method and analyzing the expired air by the Brodie method. An average of 4 menstrual cycles of each case was covered, with tests each day of the period and 3 or 4 intermenstrual determinations. An average of 37.2 cal. per sq. m. per hr. was obtained, approximately normal according to Benedict, with little variation from the normal in pre-,post-, and intermenstrual periods Only in one case, No. 4, was there a perceptible drop, i.e. 6 per cent. between the premenstrual and menstrual periods; and only in one case, No. 3, was there a postmenstrual drop, of 5 per cent. Wiltshire's conclusions agree with those of Zuntz and Blunt: that no variation in metabolism can be noted as a result of menstruation, yet do not corroborate those of Snell[8] and Rowe[9] who have observed a specific deviation from the normal due to menstruation.

Pregnancy and Puerperium.— Patients reported in the maternity ward of the Michael Reese Hospital, Chicago, the night previous to the test, thus insuring complete rest and restricted diet. Of 105 original cases[10], only 44 completed the series of consecutive readings, due to complications of pathologic conditions, tachycardia, lack of cooperation, and other factors which would of necessity make nil the value of their results. No increase could be noted in the early weeks. Beginning in the thirty-fourth week, there was a gradual rise from plus 26 per cent. to plus 33 per cent. in the fortieth week, followed by a drop to plus 15 per cent on the third day postpartum, reaching the normal level not later than the eleventh day.

Fetal sex played no important role, as an average rate in the fortieth week for the mothers bearing male fetuses was plus 37 per cent. in contrast to a plus 34 per cent. for those bearing female fetuses. The results are summarized:

1. The basal metabolic rate in 44 normal cases in late pregnancy averaged 33 to 35 per cent. above the normal for non-pregnant women of a surface area equal to the pregnant woman.

[8] Snell, A. M., Ford F., and Rowntree, L. G.: Studies in Basal Metabolism. Jour. Am. Med. Ass. 515-523, Aug., 1920.

[9] Rowe, A. H.: Monthly Fluctuations in the Normal Metabolic Rate of Men and Women. Cal. State Med. Jour. Aug., 1921.

[10] Baer, J. L.: Basal Metabolism in Pregnancy and the Puerperium. Am. Jour. Ob. and Gyne. Sept., 1921.

2. Three days after delivery the average basal metabolic rate is only 15 per cent. above normal.

3. Seven to ten days postpartum the average basal metabolic rate is approximately normal.

4. Death of the fetus in late pregnancy is detectable in a woman otherwise normal by a drop in the basal metabolic rate compared with the average in this series.

Baer presents the following conclusions:

1. The increased basal metabolic rate in late pregnancy is due to the growing demands of the fetal organism and placenta.

2. The incomplete or delayed return to normal is due to involution of the uterus and the onset of lactation.

3. Twin pregnancy should show a rate above the average for single pregnancy when both twins are well developed.

4. Thyroid enlargement may occur in pregnancy without increasing the basal metabolic rate above the average obtained in this series

5. Differential diagnosis between uterine tumor and pregnancy, will not be helped unless greater refinements in method show increased rates much earlier than in this series. The X-ray can be called on as early as the fifth month and with reasonable certainty in the sixth month.

Chronic Pulmonary Tuberculosis and Hyperthyroidism.— Studies have been made of 23 incipient, 17 moderately advanced, and 4 far advanced cases of tuberculosis, with 6 known non-tuberculous cases. In about one-third of the cases of chronic pulmonary tuberculosis, the basal metabolic rate and the blood sugar are both increased; in about one-fifth of all such cases there may be an increased basal metabolic rate and a normal blood sugar, or just the reverse, while in a much smaller percentage of cases, no change in either basal metabolic rate or blood sugar may be present: very seldom, however, would both be decreased, or even one decreased and the other normal. McBrayer[11] advances the following theory to account for the increased basal metabolic rate and blood sugar in the tuberculous cases: Tuberculotoxins stimulate the suprarenal glands, resulting in an increased output of the secretion from these glands, which in turn would do three

[11] McBrayer, R. A.: Blood Sugar and Basal Metabolism; Findings in Chronic Pulmonary Tuberculosis and Hyperthyroidism. Jour. Am. Med. Ass., Sept. 10, 1921.

things: (1) Inhibit the island of Langerhans; (2) stimulate glycolysis, and (3) stimulate the thyroid gland to greater activity, which would produce the hyperthyroid symptoms frequently encountered in incipient and chronic pulmonary tuberculosis. Thus, as hyperthyroidism will consistently manifest an increased basal metabolic rate and an increased blood sugar, McBrayer concludes that these tests can not be used for differential diagnosis.

Respiration in Pulmonary Tuberculosis.— For 5 normals McCann[12] finds the average minute volume to be 4.25 liters, average respirations were 11 per minute, and average tidal air, 397 c.c. For 5 tuberculosis patients, the average minute volume was 8.25 liters, average respiration rate 25 per minute, and average tidal air, 350 c.c. Peabody has shown that a normal may increase his tidal air up to one-third of his vital capacity. If this obtains also with a tuberculosis patient, from the tidal air of 350 c.c. a vital capacity of only 1,000 c.c. would be indicated, diminished somewhat, to be sure, by the recumbent position of the patient at the time of the test. In comparing the average minute volumes, it will be noted that the total pulmonary ventilation of the 5 cases of advanced pulmonary tuberculosis was about twice that of the normals. Yet for this increase in ventilation there was not a proportionate increase in amount of CO_2 exhaled. For a ratio of 1.2 in total minute volume, there is a CO_2 per minute production ratio of only 1:1.17. This would indicate a respiratory quotient deviating from the normal, 0.82. The respiration rate of the tuberculous was increased in each case, yet there was little rise in buccal temperature. The basal metabolic rates ranged from plus 30 per cent. to plus 3 per cent., with an average of plus 16 per cent.

Thyroxin.— Recognizing the chief function of the thyroid gland to be the generation and storage of thyroxin, Plummer[13] has formulated the following deductions in regard to the function of thyroxin:

1. Thyroxin is active directly or indirectly in the cells thruout the tissues of the body.

[12] McCann, W. S.: The Effect of the Ingestion of Foodstuffs on the Respiratory Exchange in Pulmonary Tuberculosis. Arch. Int. Med. Dec. 15, 1921.

[13] Plummer, Henry.: Interrelationship of Function of the Thyroid Gland and of its Active Agent, Thyroxin, in the Tissues of the Body. Jour. Am. Med. Ass., July 23, 1921.

2. Thyroxin is an agent hastening the rate of formation of a quantum of potential energy available for transformation on excitation of the cell.

The phenomena of hyper and hypo-activity of the thyroid gland are summarized thus:

1. Hyperthyroidism is the physiologic status of an individual otherwise normal when the thyroxin in the tissues is sufficient to hold the basal metabolism above normal.
2. Hypothyroidism is the opposite of hyperthyroidism.
3. All the phenomena in pure hyperthyroidism are those that must attend a sustained elevation of the basal metabolism.
4. The status of the hyperfunctionating adenomatous goiter is the result of a pure hyperthyroidism.
5. The status of exophthalmic goiter is not accounted for by a pure hyperthyroidism.

Experience with thyroxin administration to myxedematous patients at the Mayo Clinic has led Plummer to draw the following conclusions:

1. After the administration of a single dose of thyroxin sufficient to bring the basal metabolism to normal, the physiologic status of a thyroidless patient becomes normal in from 10 to 12 days, remains approximately normal for 10 days, and returns to the preexisting status in from 5 to 7 weeks.
2. The amount of thyroxin in the tissues (exclusive of the thyroid) of the average normal man is approximately 14 mg. Kendall, from an analysis of the iodin content in the tissues, recently estimated the amount to be 14 mg.
3. The average daily exhaustion of thyroxin in the tissues is between 0.50 and 1 mg.
4. A shift of 1 mg. of thyroxin in the tissues of the body is accompanied by a corresponding rise or fall of between 2 and 3 per cent. in the basal metabolism.
5. 14 mgs. of thyroxin given to a thyroidless person is not fully exhausted until from the end of the fifth to the eighth week.
6. 2 mgs. of thyroxin a day may hold the basal metabolism from 20 to 30 per cent. above normal; 3 mg. a day may hold the metabolism 50 per cent. above normal.

An intravenous dose of more than 1 mg. of thyroxin will, with the exception of a case of exophthalmic goiter with a basal metabolism of plus 65 per cent. or colloidal goiter with bruit cause a sustained elevation in the metabolic rate. It has been found, however, that daily doses of 1 mg. of thyroxin for months to persons with an apparently normal thyroid have caused on deflection in the basal metabolism.

The daily exhaustion of thyroxin of a thyroidless patient is from 0.2 to 0.4 mg., as compared with 0.5 to 1.0 for the normal. The oral dose necessary to keep the basal metabolism of the myxedematous patient at the normal level is 1.6 mg., much in excess of the theoretical elimination of thyroxin. This is accounted for, possibly, by the incomplete absorption of thyroxin from the gastrointestinal tract; thus the metabolic reaction is more intense and more constant with intravenous administration; a fact, incidentally, in favor of the use of thyroxin instead of desiccated thyroid.

Pituitary Extract.— Experiments were performed[14] upon 4 groups of individuals; normals, hypothyroids, those with pituitary disorders, and normal and hypothyroid cases who had received thyroxin. The object was to determine the effect that extract of the posterior lobe of the hypophysis, when used subcutaneously, had on the metabolism of the normal and of those with endocrine disturbances, chiefly of the thyroid and pituitary glands. Any relation between thyroxin, the active principle of the thyroid gland, and pituitary extract, was to be noted.

Of 12 students, none manifesting signs of endocrine disturbance, with a normal basal metabolism, 11 responded with an increase after the use of pituitary extract. The percentile increase in basal metabolism varied from 2 to 16, and averaged 5. Physiological changes have been apparent; marked pallor, slight systolic elevation in the blood pressure, and subjectively abdominal cramps.

In the group of 4 clearly defined cases of hypothyroidism, there was a decrease in the heat production after administration of the pituitary extract. There were fewer subjective symptoms in this group. A synergy between the thyroid and hypophysis would be evidenced by the comparison of results of pituitary treatment on the normals, on the one hand, in which there was an acceleration of heat production, and on the hypothyroids,

[14] McKinlay, C. A.: The Effect of the Extract of the Posterior Lobe of the Pituitary on Basal Metabolism in Normal Individuals and in those with Endocrine Disturbances. Arch. Int. Med. **28**: 703-710, Dec. 15, 1921.

on the other hand, in which there was a slight but consistent abatement of heat production.

In the group of 3 cases with a normal thyroid, judged from the absence of myxedematous symptoms, there was a disturbed function of the hypophysis, evidenced by the development of obesity, increased sugar tolerance, subnormal temperature, and dysmenorrhea in one of them. Pituitary extract accelerated the heat production in each case. McKinlay suggests that if such a relationship, viz., that of an increase in metabolism with pituitary extract only if the thyroid is active, holds true in a larger series of cases, the determination of the effect of pituitary extract on basal metabolism may be used as a test to estimate in pluriglandular cases the extent, if any, of thyroid involvement.

With the last group of 6 cases, 4 of whom were normals to which thyroxin had been administered, and 2 hypothyroids who had been receiving benefit from thyroxin, there was a corroboration of the preceding hypothesis. The normals reacted with an increased heat production, slightly greater than the first group of normals who had had no thyroxin. The myxedematous patients showed no response to pituitary extract. McKinlay believes the experiment to give evidence that heat production of the body is due to a balance between endocrine glands, more specifically between the thyroid and hypophysis. The following conclusions are presented:

1. Normal persons responded quite constantly with increased basal metabolism following the subcutaneous injection of pituitary extract.

2. In a small series of cases with hypothyroidism, the basal metabolism was diminished rather than increased, which suggests that pituitary extract is effective in accelerating heat production only of a normally functioning thyroid gland.

3. In four cases with subnormal basal metabolism in which clinical evidence of myxedema was lacking and preponderance of influence of endocrine glands other than thyroid was suggested, the positive response to pituitary extract was present.

4. The increased acceleration of basal metabolism in a group of normal individuals following the subcutaneous injection of pituitary extract one week after an injection of thyroxin, is interpreted as suggesting a synergic action between thyroxin and pituitary extract.

Dysfunction of the Liver.— Aub and Means[15] report a normal basal metabolism on 12 patients with distinct involvement of the liver, representing varied types of disorders. The reaction to ingestion of protein food with the patients was much the same as with normals. Even in a case of portal obstruction with rapidly recurring ascites, and also a case with practically complete bile duct obstruction, the normal elevation of the metabolism was noted. Protein catabolism was more evident in cirrhosis in general, altho in two cases of cirrhosis and one of gallstones, there was no specific rise in metabolism. Aub and Means conclude:

1. That in these cases the basal metabolism of liver disease was essentially within normal limits. The liver, is, therefore, either not an important regulator of the metabolic rate, or it is adequate for this purpose even when severely diseased.
2. The rate of absorption and utilization of protein in large quantities was usually normal.
3. The conclusion seems justified that either the liver is not the main seat of the specific dynamic action of protein or that it can adequately perform that function even in disease.
4. The observation of Du Bois that in exophthalmic goiter a normal increase in heat production, due to protein, is superimposed on the high basal rate is confirmed.

Myelogenous Leucemia.— Gunderson[16] reports a consistently high metabolism on 19 cases of myelogenous leucemia with 62 observations. Altho he does not find that the increase in metabolism and the degree of leucocytosis vary in direct proportion, the former at least bears as close a relation to the number of immature white cells in the blood as it does to the total leucocyte count. The increase in metabolism above normal might be attributed to the anemia of varying degrees, present in all cases. Gunderson points out that at the most the anemia would be responsible for only a slight increase, and cites the following cases: On Jan. 11, the basal metabolism was plus 80 per cent. the hemoglobin 32 per cent., white count 240,000 per cu. mm., myelocytes 58 per cent., and the myeloblasts,

[15] Aub, J. C., and Means, J. H.: The Basal Metabolism and the Specific Dynamic Action of Protein in Liver Disease. Arch. Int. Med., Aug. 15, 1921.

[16] Gunderson, A. H.: The Basal Metabolism in Myelogenous Leucemia and its Relation to the Blood Findings. Boston Sur. and Med. Jour., Dec. 29, 1921.

FIG. 1 NORMAL

FIG. 2 HYPERPNEA

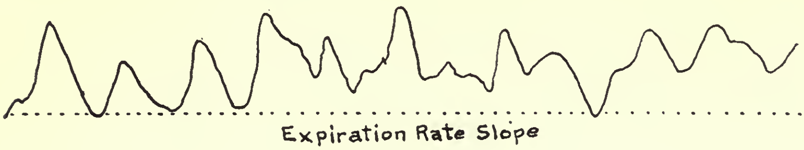


FIG. 3

Same Patient as Fig. 2

FIG. 4

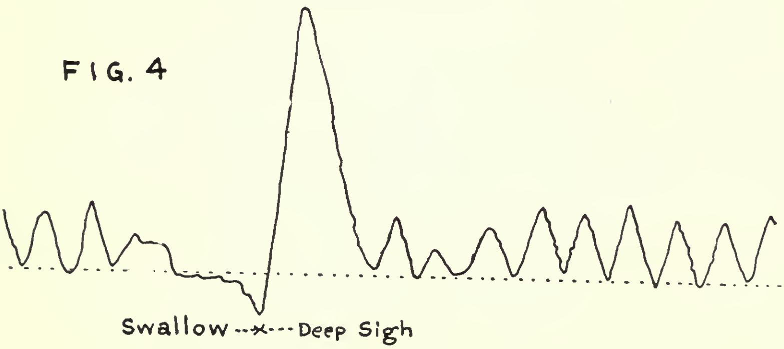
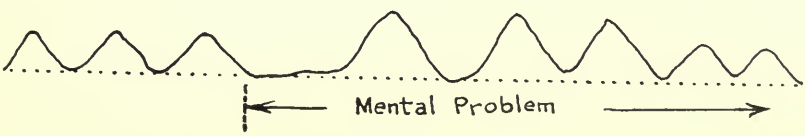


FIG. 5



30 per cent. On March 26, the basal metabolism was plus 34 per cent., hemoglobin 40 per cent., leucocyte 235,000, myelocytes 30 per cent., and the myeloblasts 3 per cent. The basal metabolism may then be used as an index of the activity of the leucopoetic tissue, as the results of these observations show that it bears a relation particularly to the number of immature white cells in the blood stream, regardless of the total leucocytosis. The highest values for the basal metabolism are usually found in cases with very high white counts and many myelocytes, or in cases showing high percentages of myeloblasts. Gunderson reports that in exactly half of the 62 determinations, the metabolic rate was over plus 20. The case stated above, however, had the maximum rate, plus 80.

Kymograf Records.— Records of respirations afford a grafic representation of respirations — a picture of respiratory processes from the beginning to the end of the test. These records may show the regularity, frequency and depth of respirations, and give a check on the rate of respiration and the rate of accumulation of expired air, or the rate of consumption of oxygen.

The Kymograf records here shown have been obtained by a new form of recorder or kymograf that is directly attacht to an ordinary form of Benedict Metabolism Apparatus. The records are made in ink on a strip of paper 2¼″ wide (ordinary adding machine paper) that is driven by a clock mechanism, and is wound on to one roll from another. A continuous record of a patient's respiration may thus be obtained covering many minutes, and extended on a strip of paper 10 to 20 feet long. The time mark is made every minute, or every fifth of a second. The marks are not shown in Figures 1 to 5 that are given on page 235, which illustrate the records of respirations for normal conditions as well as those resulting from certain irregularities.

Figure 1 shows the record of a normal person in whom there was no element of fear of the apparatus, or apprehension of the test. In fact, a mechanic who had worked upon the apparatus for over a year was chosen for this test. It will be noted that there is a slight apneoic flatness of the curve at the base. The amplitude is, however, by no means exact, nor is the height. This is the usual type in records of composed patients. The frequency of respirations per minute, which is not shown by this portion of the curve, remains constant. The dotted line has been added to the record and represents the respiration rate slope and enables one to determine rate of oxygen consumption.

Figure 2 shows the record of the respirations of a girl who has been familiar with metabolism apparatus for a year. Altho purposely no attempt was made to allay her fears, or to comfort her in any way, one would at least expect her curve to become more regular after she had been attacht to the apparatus for a few minutes. This portion of the curve represents the last of an 8 minute period. It is obvious that any reading taken during this period would be invalid, as not the slightest consistency is seen even at the expiration rate slope line.

Figure 3 shows test on the same girl, made the following day. The respirations became more regular in every respect, altho there was a slight increase in respiration rate. A wave at the expiration base line is evident, which would indicate hyperpnea rather than dyspnea.

Figure 4 illustrates the effect of swallowing. When metabolism tests are made with closed circuit apparatus, many authorities have stated that an error may occur in the amount of oxygen consumption if the patient swallows oxygen. They have also believed that carbon dioxid would be washed out of the respiratory system as a result of the unnatural respirations that are brought about while the nose is clamped, as breathing into the closed circuit takes place thru the mouth only.

Figure 4, however, shows that in the case of a deep swallow there is immediate return to the expiration rate slope line, and thus normal conditions resumed much more quickly than is generally supposed.

Figure 5, illustrates the discrepancy of respiration that may be caused by a mental problem. A problem in oral arithmetic was given to the patient, such as — "Multiply 6 by 2, add 6, divide by 3, add 6, add 1, subtract 11, multiply by 5, etc." At the onset of the problem there was evidence of a distorted curve from the normal, due to the concentration of the subject upon the mathematics. The entire curve during the time of mental exertion was irregular in all respects, returning quickly to the normal at the end.

Grafic records are a distinct aid in making metabolism determinations and analyzing the results of tests. It is probable that such records will come into more extended use in the future.

CHAPTER 28

TABLES WITH EXPLANATIONS

This chapter contains "Computations", which are the terror of many a successful physician and the joy of many a laboratory assistant. However, the average physician or technician need have little fear of having difficulty in understanding the requisite processes of computation if he will content himself with following the simplified methods that are given. Each section has both a simplified process and a more complete and accurate process.

There are Normal Standards of Basal Metabolism; a simplified table of Normal Consumption of Oxygen; Values of Body Surface Area by direct readings from a table, a chart, and by computation; the Methods of correcting for Temperature, Barometer, and Saturation; and Tables of Equivalents.

Determination of Normal Basal Metabolism.— The Du Bois Normal Standards of Basal Metabolism with 1.8 calories subtracted from each value are given below. (See Means, J. H.— Archives of Internal Medicine, May 1921.)

AVERAGE CALORIES PER HOUR PER SQUARE METER OF BODY SURFACE, AND THE VOLUME OF OXYGEN PER MINUTE EQUIVALENT OF THE CALORIES

Age	*Cals. Males*	*Log. of Cals.*	*Oxygen C. C. Per Minute*	*Log. of C. C.*	*Cals. Females*	*Log. of Cals.*	*Oxygen C. C. Per Minute*	*Log. of C. C.*
14-16	44.2	1.6454	153	2.1847	41.2	1.6149	142	2.1523
16-18	41.2	.6149	142	.1523	38.2	.5821	132	.1206
18-20	39.2	.5933	135	.1303	36.2	.5587	125	.0969
20-30	37.7	.5763	130	.1139	35.2	.5465	122	.0864
30-40	37.7	.5763	130	.1139	34.7	.5403	120	.0792
40-50	36.7	.5647	127	.1038	34.2	.5340	118	.0719
50-60	35.7	.5527	123	.0899	33.2	.5211	115	.0607
60-70	34.7	.5403	120	.0792	32.2	.5079	111	.0453
70-80	33.7	.5276	116	.0645	31.2	.4942	108	.0334

NORMAL STANDARDS OF BASAL METABOLISM FOR BOYS AND GIRLS OF WEIGHTS 20 TO 38 KILOS*

(Ages 6 to 12 years approximately)

Weight is determining factor for basal metabolism of boys and girls

Body Weight (without clothing)		Heat Production in Calories per 24 hours		Oxygen Consumption in Cubic Centimeters per minute	
Kilos	Pounds	Boys	Girls	Boys	Girls
20.0	44	860	805	124	116
20.5	45	873	818	126	118
21.0	46	885	830	127	120
21.5	47	898	842	129	121
22.0	48	910	855	131	123
22.5	50	925	867	133	125
23.0	51	940	880	135	127
23.5	52	953	890	137	128
24.0	53	965	900	139	130
24.5	54	978	915	141	132
25.0	55	990	930	143	134
25.5	56	1005	940	145	135
26.0	57	1020	950	147	137
26.5	58	1033	962	149	139
27.0	59	1045	975	150	140
27.5	61	1058	987	152	142
28.0	62	1070	1000	154	144
28.5	63	1080	1010	155	145
29.0	64	1090	1020	157	147
29.5	65	1103	1032	159	149
30.0	66	1115	1045	161	150
30.5	67	1127	1058	162	152
31.0	68	1140	1070	164	154
31.5	69	1150	1080	166	155
32.0	70	1160	1090	167	157
32.5	72	1170		168	
33.0	73	1180		170	
33.5	74	1190		171	
34.0	75	1200		173	
34.5	76	1210		174	
35.0	77	1220		176	
35.5	78	1230		177	
36.0	79	1240		179	
36.5	80	1248		180	
37.0	81	1255		181	
37.5	83	1265		182	
38.0	84	1275		184	

* Predicted standards. Prepared by editor from Table 36 in Benedict and Talbot's "Metabolism from Birth to Puberty." Carnegie Institute of Washington, Washington, D. C., 1921.

Examples illustrating the method of using foregoing tables: Male, 32 years old; height, 160 cm.; weight, 67 kg. From the table on page 238 it is obvious that a man 32 years old would have a normal basal metabolism of 37.7 calories per hour for each square meter of his body surface. The method of computing the body surface of this particular patient is explained in the pages that follow. It will be seen that his body-surface area is 1.70 square meters; therefore his total basal metabolism is 37.7 × 1.70 or 64.1 calories per hour. By referring to the table on page 272, the equivalent of 64.1 calories per hour is 221 c. c. of oxygen per minute.

A girl weighing 50 lbs.: from the table it is readily seen that the normal heat production is 867 calories per 24 hours and the normal oxygen consumption is 125 c. c. per minute.

For the Carbon Dioxid Method the following Standards for Normal Carbon Dioxid Elimination are proposed by Dr. J. T. King, Jr.

CARBON DIOXID ELIMINATION PER HOUR PER SQUARE METER OF BODY SURFACE

Age Years	*Males Grams*	*Females Grams*
15-20	14.03	12.75
20-30	12.98	11.95
30-40	12.86	11.85
40-50	12.52	11.74
50-60	12.21	11.37
60-70	11.86	11.05
70-80	11.53	10.71

Normal consumption of oxygen may be determined by simply selecting the proper value from the table which follows and making minor corrections, or by accurate computations as explained later.

The table and explanations of the simplified method are given on the following three pages. The values given in the table are based on Du Bois' Normal Standards with a slight modification: Instead of 37.7 calories and 36.7 for the ages of 20 to 50 as given in the preceding table, a mean value of 37.4 is used. For ages other than 20 to 50, the corrections are based on the Du Bois values and exprest in per cent. as shown on the next page.

Table Shows
NORMAL CONSUMPTION OF OXYGFN

At 0° Temperature and 760 mm. Barometer Pressure,

in Cubic Centimeters per Minute

under Basal Conditions.

Sex and Age Corrections for Volumes in Tables.

Males: Ages 20 to 50, no correction.

16 to 18, add 1 per cent. to volumes in table
18 to 20, add 5 per cent. to volumes in table
50 to 60, subtract 4 per cent. from volumes in table
60 to 70, subtract 7 per cent. from volumes in table

Females: Compute for a Male of same age and subtract 7 per cent.

Examples (To find Normal Consumption of Oxygen for)

1. Male, 32 years old, weight 67 kilograms, height 160 centimeters. From table volume is 220 cubic centimeters per minute.
2. Female, 28 years old, weight 147 pounds, height 65 inches. From table volume 221 cc. per minute. Subtract 7 per cent. for Sex Correction, 208 cc. per minute.
3. Female, 16 years old, weight 94 pounds, height 60 inches. From table, 185 cc. per minute. Add 10 per cent. for Age Correction, 193 cc. Subtract 7 per cent. for Sex Correction, 179 cc. normal consumption of oxygen per minute.

NOTE:—The values given for the Normal Consumption of Oxygen have been prepared by Prof. Frank B. Sanborn.

(1) From table of calories given by Drs. Aub and DuBois in "The Basal Metabolism of Old Men" (Archives of Internal Medicine, 1919.) with 1.8 calories subtracted. (See Means, J. H., Arch. Int. Med. May, 1921.)

(2) Using an average value of 4.83 calories per liter of oxygen.

(3) An average normal respiratory quotient of 0.82.

(4) DuBois formula of Body Surface, which is:

$$\text{Area (sq. cm.) equals } 71.84 \times (\text{height in cm.})^{0.725} \times (\text{weight in kg.})^{0.425}$$

HEIGHT IN CENTIMETERS

WEIGHT IN KILOGRAMS	140	145	150	155	160	165	170	175	180	185	190	WEIGHT IN POUNDS
30	142	145	149	152	156	159	163	166	170	173	177	66
1	144	147	151	154	158	161	165	168	172	175	179	68
2	145	149	153	156	160	163	167	170	174	177	181	70
3	147	151	155	158	162	165	169	173	177	180	184	73
4	149	153	157	160	164	167	171	175	179	182	186	75
5	151	155	159	162	166	170	174	177	181	184	188	77
6	153	157	161	164	168	172	176	179	183	187	191	79
7	155	159	163	166	170	174	178	182	185	189	193	81
8	156	161	164	168	172	176	180	184	188	191	195	84
9	158	162	166	170	174	178	182	186	190	194	198	86
40	159	164	168	172	176	180	184	188	192	196	200	88
1	161	165	169	174	179	182	186	190	194	198	202	90
2	162	167	171	176	181	184	188	192	196	200	204	92
3	164	169	173	178	182	185	189	194	198	202	206	95
4	165	170	175	180	184	187	191	196	200	204	208	97
5	167	172	177	181	186	189	193	198	201	205	210	99
6	169	174	179	183	188	191	195	200	203	207	212	101
7	171	176	180	184	189	192	197	202	205	209	214	103
8	172	177	182	186	191	194	199	204	207	211	216	106
9	174	179	183	188	192	196	201	206	209	213	218	108
50	176	181	185	189	193	197	202	207	211	215	220	110
1	178	183	186	191	195	199	204	209	212	217	221	112
2	179	184	188	192	196	200	205	211	214	219	223	114
3	181	186	189	194	198	202	207	212	216	220	225	117
4	182	187	191	195	199	203	208	214	217	222	227	119
5	184	188	193	197	201	205	210	216	219	224	228	121
6	185	189	194	199	203	207	212	218	221	226	230	123
7	186	191	196	200	205	209	213	219	222	228	232	125
8	188	192	197	202	206	210	215	221	224	229	233	128
9	189	194	199	203	208	212	216	222	226	231	235	130
60	190	195	200	204	209	213	217	223	228	233	237	132
1	191	196	201	206	211	215	219	225	230	235	239	134
2	192	198	202	207	212	216	220	226	231	236	240	136
3	193	199	203	209	214	218	222	228	233	238	242	139
4	195	200	205	210	215	219	223	229	234	239	243	141
5	196	201	206	212	217	221	225	231	236	241	245	143
6	197	202	207	213	218	222	227	232	237	242	247	145
7	199	204	209	215	220	224	228	234	239	244	249	147
8	200	205	210	216	221	225	230	235	240	245	250	150
9	201	207	212	218	222	227	231	237	242	247	252	152
70	202	208	213	218	223	228	233	238	243	248	253	154
1	203	209	214	219	224	229	235	240	245	250	255	156
2	204	210	216	220	225	231	236	241	246	251	256	158
3	206	212	217	222	227	232	238	243	248	253	258	161
4	207	213	219	223	228	234	239	244	249	254	259	163
5	208	214	220	224	229	235	241	246	251	256	261	165
6	209	215	221	225	230	236	242	247	252	257	263	167
7	210	216	222	227	232	238	244	249	254	259	264	169
8	212	218	224	228	233	239	245	250	255	260	266	172
9	213	219	225	230	235	240	246	251	257	262	267	174
80	214	220	226	231	236	241	247	253	258	263	268	176
1	215	222	227	232	237	242	248	254	259	264	270	178
2	217	223	228	234	239	244	250	256	261	266	271	180
3	218	225	230	235	240	245	251	257	262	267	273	183
4	220	226	231	237	242	247	253	259	264	269	274	185
5	221	227	233	238	243	248	254	260	265	270	276	187
6	222	228	234	239	244	249	255	261	266	271	277	189
7	223	229	235	240	246	251	256	262	268	273	279	191
8	224	230	236	242	247	252	258	264	269	274	280	194
9	225	231	237	243	248	254	259	265	271	276	282	196
	55	57	59	61	63	65	67	69	71	73	75	

HEIGHT IN INCHES

HEIGHT IN CENTIMETERS

WEIGHT IN KILOGRAMS	150	155	160	165	170	175	180	185	190	195	200	WEIGHT IN POUNDS
90	238	244	249	255	260	266	271	276	282	287	292	198
1	239	245	250	256	261	267	272	277	283	288	293	200
2	240	246	251	257	262	268	273	278	284	289	294	202
3	241	247	252	258	264	269	275	280	286	291	296	205
4	242	248	253	259	265	270	276	281	287	292	297	207
5	243	249	254	260	266	271	277	282	288	293	298	209
6	244	250	255	261	267	272	278	283	289	294	299	211
7	245	251	256	263	269	274	279	284	290	295	300	213
8	246	252	258	264	270	275	281	286	292	297	302	216
9	247	253	259	266	271	277	282	287	293	298	303	218
100	248	254	260	267	272	278	284	289	294	299	304	220
1	249	255	261	268	273	279	285	290	295	300	305	222
2	250	256	262	269	274	280	286	292	297	302	307	224
3	251	257	263	270	275	281	288	293	298	303	308	227
4	252	258	264	271	276	282	289	294	299	304	309	229
5	253	260	266	272	278	284	290	296	301	306	311	231
6	254	261	267	273	279	285	291	297	302	307	312	233
7	255	262	268	274	280	286	293	298	303	308	313	235
8	256	263	269	275	281	287	294	300	305	310	315	238
9	257	264	270	276	282	288	295	301	306	311	316	240
110	258	265	271	277	283	289	296	302	307	312	317	242
1	259	266	272	278	284	290	297	303	308	313	318	244
2	260	267	273	279	285	291	298	304	309	315	320	246
3	261	268	274	280	286	293	299	305	310	316	321	249
4	262	269	275	281	287	294	300	306	312	317	322	251
5	263	270	276	283	289	295	302	308	313	319	324	253
6	264	271	277	284	290	296	303	309	314	320	325	255
7	265	272	278	285	291	298	304	310	315	321	326	257
8	266	273	279	286	292	299	305	311	317	323	328	260
9	267	274	280	287	293	300	306	312	318	324	329	262
120	268	275	281	288	294	301	307	313	319	325	330	264
1	269	276	282	289	295	302	308	314	320	326	331	266
2	270	277	283	290	296	303	309	315	321	327	332	268
3	271	278	284	291	297	304	310	316	322	328	333	271
4	272	279	285	292	298	305	311	317	323	329	335	273
5	272	279	285	292	299	306	312	319	325	331	336	275
6	273	280	286	293	300	307	313	320	326	332	337	277
7	274	281	287	294	301	308	314	321	327	333	339	279
8	275	282	288	295	302	309	315	322	328	334	340	282
9	276	283	289	296	303	310	316	323	329	335	341	284
130	277	284	290	297	304	311	317	324	330	336	342	286
1	278	285	291	298	305	312	318	325	331	337	343	288
2	279	286	292	299	306	313	319	326	332	338	344	290
3	280	287	293	300	307	314	320	327	333	339	345	293
4	281	288	294	301	308	315	321	328	334	340	346	295
5	281	288	294	302	309	316	323	329	335	341	347	297
6	282	289	295	303	310	317	324	330	336	342	348	299
7	283	290	296	304	311	318	325	331	337	343	349	301
8	284	291	297	305	312	319	326	332	338	344	350	304
9	285	292	298	306	313	320	327	333	339	345	351	306
140	286	293	299	307	314	321	328	334	340	346	352	308
1	287	294	300	308	315	322	329	335	341	347	353	310
2	288	294	301	309	315	323	329	336	342	348	354	312
3	289	295	302	310	316	324	330	337	343	349	355	315
4	289	296	303	311	317	325	331	338	344	350	356	317
5	290	297	304	312	318	326	332	339	345	351	357	319
6	291	298	305	313	319	327	333	339	346	352	358	321
7	291	299	306	314	320	328	334	340	346	353	359	323
8	292	300	307	315	321	329	335	341	347	354	360	326
9	293	301	307	315	322	329	336	342	348	355	361	328
	59	61	63	65	67	69	71	73	75	77	79	

HEIGHT IN INCHES

Body Surface Area affords another method of estimating the Normal Basal Metabolism of an individual. The tables given on the preceding pages include Body Surface Area as a factor which is fully taken into account when the tables are prepared, but in the pages that follow explanation is given of the intermediate steps by which Body Surface Area is determined and this combined with normal calories per unit of area gives the Normal Basal Metabolism.

Body Surface Area may be found by the following table and chart that have been prepared from the Du Bois formula for Body Surface, which is

$$A = 71.84 \times Wt.^{0.425} \times Ht.^{0.725}$$

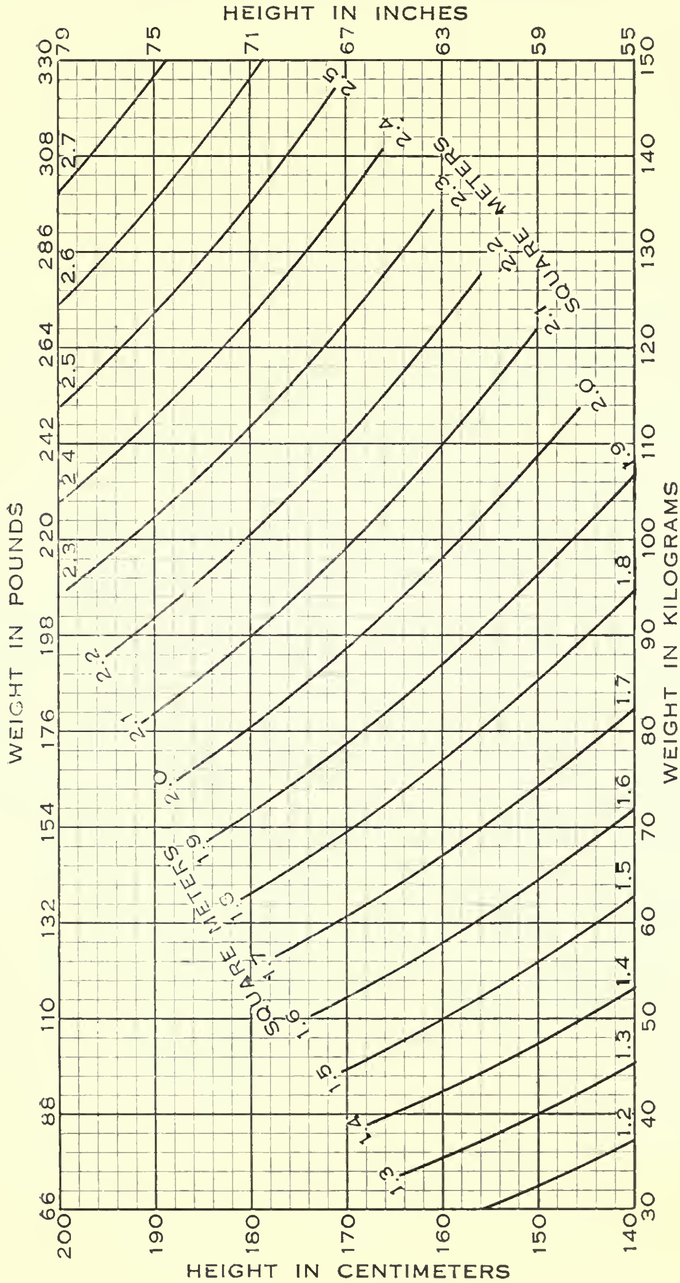
A is the area in square centimeters; *Ht.*, the height in centimeters, and *Wt.*, the weight in kilograms. Altho the formula gives the area in square centimeters, in the table and chart it is exprest in square meters. (10,000 sq. cm. = 1 sq. m.).

Examples of Body Surface Area as obtained from the Tables: (Similar values may also be obtained from the chart on page 245)

1. A person 172 centimeters in height, weighing 62 kilograms. From the table the Body Surface Area is 1.74 square meters.
2. A person 70 inches in height, weighing 148 pounds. From the table the Body Surface Area is 1.84 square meters.
3. A person 74 inches in height, weighing 285 pounds. From the table the Body Surface Area is 2.53 square meters.

The tables and also the Body Surface Chart, which are given on the pages that follow include values for all persons whose height or weight is not extreme.

BODY SURFACE CHART



Plotted from the DuBois new formula for Body Surface which is: Area in square centimeters equals Constant 71.84 times Weight of person in kilograms raised to the 0.425 power, times Height in centimeters raised to the 0.725 power.

HEIGHT IN CENTIMETERS

WEIGHT IN KILOGRAMS / WEIGHT IN POUNDS

	140	145	150	155	160	165	170	175	180	185	190	
30	1.09	1.12	1.15	1.18	1.21	1.24	1.26	1.29	1.32	1.34	1.37	66
1	1.11	1.14	1.17	1.20	1.23	1.25	1.28	1.31	1.33	1.36	1.39	68
2	1.13	1.16	1.19	1.21	1.24	1.27	1.30	1.33	1.35	1.38	1.41	70
3	1.14	1.17	1.20	1.23	1.26	1.29	1.31	1.34	1.37	1.40	1.42	73
4	1.16	1.19	1.22	1.25	1.28	1.30	1.33	1.36	1.39	1.42	1.44	75
5	1.17	1.20	1.23	1.26	1.29	1.32	1.35	1.38	1.40	1.43	1.46	77
6	1.18	1.21	1.25	1.28	1.31	1.33	1.36	1.39	1.42	1.45	1.48	79
7	1.20	1.23	1.26	1.29	1.33	1.35	1.38	1.41	1.44	1.47	1.49	81
8	1.21	1.24	1.27	1.31	1.34	1.37	1.40	1.43	1.45	1.48	1.51	84
9	1.23	1.26	1.29	1.32	1.35	1.38	1.41	1.44	1.47	1.50	1.53	86
40	1.24	1.27	1.30	1.34	1.37	1.40	1.43	1.46	1.49	1.52	1.55	88
1	1.25	1.28	1.31	1.35	1.38	1.41	1.44	1.47	1.50	1.53	1.56	90
2	1.26	1.30	1.33	1.36	1.39	1.43	1.46	1.49	1.52	1.55	1.58	92
3	1.28	1.31	1.34	1.38	1.41	1.44	1.47	1.50	1.53	1.56	1.59	95
4	1.29	1.32	1.35	1.39	1.42	1.45	1.48	1.52	1.55	1.58	1.60	97
5	1.30	1.34	1.37	1.40	1.43	1.47	1.50	1.53	1.56	1.59	1.62	99
6	1.32	1.35	1.38	1.42	1.45	1.48	1.51	1.55	1.58	1.61	1.63	101
7	1.33	1.36	1.39	1.43	1.46	1.50	1.53	1.56	1.59	1.62	1.65	103
8	1.34	1.38	1.41	1.44	1.47	1.51	1.54	1.58	1.61	1.64	1.66	106
9	1.35	1.39	1.42	1.46	1.49	1.52	1.55	1.59	1.62	1.65	1.68	108
50	1.36	1.40	1.43	1.47	1.50	1.54	1.57	1.61	1.64	1.67	1.70	110
1	1.37	1.41	1.44	1.48	1.51	1.55	1.58	1.62	1.65	1.68	1.71	112
2	1.38	1.42	1.46	1.49	1.52	1.56	1.59	1.63	1.66	1.70	1.73	114
3	1.40	1.44	1.47	1.51	1.54	1.58	1.61	1.65	1.68	1.71	1.74	117
4	1.41	1.45	1.48	1.52	1.55	1.59	1.62	1.66	1.69	1.72	1.75	119
5	1.42	1.46	1.49	1.53	1.56	1.60	1.63	1.67	1.70	1.74	1.77	121
6	1.43	1.47	1.50	1.54	1.57	1.61	1.64	1.68	1.72	1.75	1.78	123
7	1.44	1.48	1.52	1.56	1.59	1.63	1.66	1.70	1.73	1.76	1.79	125
8	1.45	1.49	1.53	1.57	1.60	1.64	1.67	1.71	1.74	1.78	1.81	128
9	1.46	1 50	1.54	1.58	1.61	1.65	1.68	1.72	1.75	1.79	1.82	130
60	1.47	1.51	1.55	1.59	1.62	1.66	1.69	1.73	1.77	1.81	1.84	132
1	1.48	1.52	1.56	1.60	1.63	1.67	1.71	1.75	1.78	1.82	1.85	134
2	1.49	1.53	1.57	1.61	1.64	1.68	1.72	1.76	1.79	1.83	1.86	137
3	1.50	1.54	1.58	1.62	1.66	1.70	1.73	1.77	1.80	1.84	1.88	139
4	1.51	1.55	1.59	1.63	1.67	1.71	1.74	1.78	1.82	1.86	1.89	141
5	1.52	1.56	1.60	1.64	1.68	1.72	1.75	1.79	1.83	1.87	1.90	143
6	1.53	1.57	1.61	1.65	1.69	1.73	1.76	1.80	1.84	1.88	1.91	145
7	1.54	1.58	1.62	1.66	1.70	1.74	1.78	1.82	1.85	1.89	1.93	147
8	1.55	1.59	1.63	1.67	1.71	1.75	1.79	1.83	1.86	1.90	1.94	150
9	1.56	1.60	1.64	1.68	1.72	1.76	1.80	1.84	1.87	1.91	1.95	152
70	1.57	1.61	1.65	1.69	1.73	1.77	1.81	1.85	1.89	1.93	1.96	154
1	1.58	1.62	1.66	1.70	1.74	1.78	1.82	1.86	1.90	1.94	1.97	156
2	1.59	1.63	1.67	1.71	1.75	1.79	1.83	1.87	1.91	1.95	1.98	158
3	1.60	1.64	1.68	1.72	1.76	1.80	1.84	1.88	1.92	1.96	2.00	161
4	1.61	1.65	1.69	1.73	1.77	1.81	1.85	1.89	1.93	1.97	2.01	163
5	1.62	1.66	1.70	1.74	1.78	1.82	1.86	1.90	1.94	1.98	2.02	165
6	1.63	1.67	1.71	1.75	1.79	1.83	1.87	1.91	1.95	1.99	2.03	167
7	1.63	1.68	1.72	1.76	1.80	1.84	1.88	1.92	1.96	2.00	2.04	169
8	1.64	1.69	1.73	1.77	1.81	1.85	1.89	1.93	1.97	2.01	2.05	172
9	1.65	1.70	1.74	1.78	1.82	1.86	1.90	1.95	1.99	2.03	2.06	174
80	1.66	1.71	1.75	1.79	1.83	1.87	1.91	1.96	2.00	2.04	2.08	176
1	1.67	1.72	1.76	1.80	1.84	1.88	1.92	1.97	2.01	2.05	2.09	178
2	1.68	1.73	1.77	1.81	1.85	1.89	1.93	1.98	2.02	2.06	2.10	180
3	1.69	1.74	1.78	1.82	1.86	1.90	1.94	1.99	2.03	2.07	2.11	183
4	1.70	1.75	1.79	1.83	1.87	1.91	1.95	2.00	2.04	2.08	2.12	185
5	1.70	1.75	1.80	1.84	1.88	1.92	1.96	2.01	2.05	2.09	2.13	187
6	1.71	1.76	1.80	1.85	1.89	1.93	1.97	2.02	2.06	2.10	2.14	189
7	1.72	1.77	1.81	1.86	1.90	1.94	1.98	2.03	2.07	2.11	2.15	191
8	1.73	1.78	1.82	1.87	1.91	1.95	1.99	2.04	2.08	2.12	2.16	194
9	1.74	1.79	1.83	1.88	1.92	1.96	2.00	2.05	2.09	2.13	2.17	196
	55	57	59	61	63	65	67	69	71	73	75	

HEIGHT IN INCHES

HEIGHT IN CENTIMETERS

WEIGHT IN KILOGRAMS	150	155	160	165	170	175	180	185	190	195	200	WEIGHT IN POUNDS
90	1.84	1.89	1.93	1.97	2.01	2.06	2.10	2.14	2.18	2.22	2.26	198
1	1.85	1.90	1.94	1.98	2.02	2.07	2.11	2.15	2.19	2.23	2.27	200
2	1.86	1.90	1.95	1.99	2.03	2.08	2.12	2.16	2.20	2.24	2.28	202
3	1.86	1.91	1.96	2.00	2.04	2.09	2.13	2.17	2.21	2.25	2.29	205
4	1.87	1.92	1.97	2.01	2.05	2.10	2.14	2.18	2.22	2.26	2.30	207
5	1.88	1.93	1.97	2.02	2.06	2.11	2.15	2.19	2.23	2.27	2.31	209
6	1.89	1.94	1.98	2.03	2.07	2.12	2.16	2.20	2.24	2.28	2.32	211
7	1.90	1.95	1.99	2.04	2.08	2.13	2.17	2.21	2.25	2.29	2.33	213
8	1.91	1.96	2.00	2.05	2.09	2.14	2.18	2.22	2.26	2.30	2.34	216
9	1.91	1.96	2.01	2.06	2.10	2.15	2.19	2.23	2.27	2.31	2.35	218
100	1.92	1.97	2.02	2.07	2.11	2.16	2.20	2.24	2.28	2.32	2.36	220
1	1.93	1.98	2.03	2.08	2.12	2.17	2.21	2.25	2.29	2.33	2.37	222
2	1.94	1.99	2.04	2.09	2.13	2.18	2.22	2.26	2.30	2.34	2.38	224
3	1.94	1.99	2.04	2.09	2.13	2.18	2.23	2.27	2.31	2.35	2.39	227
4	1.95	2.00	2.05	2.10	2.14	2.19	2.24	2.28	2.32	2.36	2.40	229
5	1.96	2.01	2.06	2.11	2.15	2.20	2.24	2.29	2.33	2.37	2.41	231
6	1.97	2.02	2.07	2.12	2.16	2.21	2.25	2.30	2.34	2.38	2.42	233
7	1.98	2.03	2.08	2.13	2.17	2.22	2.26	2.31	2.35	2.39	2.43	235
8	1.98	2.03	2.08	2.13	2.17	2.22	2.27	2.32	2.36	2.40	2.44	238
9	1.99	2.04	2.09	2.14	2.18	2.23	2.28	2.33	2.37	2.41	2.45	240
110	2.00	2.05	2.10	2.15	2.19	2.24	2.29	2.34	2.38	2.42	2.46	242
1	2.01	2.06	2.11	2.16	2.20	2.25	2.30	2.35	2.39	2.43	2.47	244
2	2.02	2.07	2.12	2.17	2.21	2.26	2.31	2.36	2.40	2.44	2.48	246
3	2.02	2.07	2.12	2.17	2.22	2.27	2.32	2.37	2.41	2.45	2.49	249
4	2.03	2.08	2.13	2.18	2.23	2.28	2.33	2.38	2.42	2.46	2.50	251
5	2.04	2.09	2.14	2.19	2.23	2.28	2.33	2.38	2.42	2.47	2.51	253
6	2.05	2.10	2.15	2.20	2.24	2.29	2.34	2.39	2.43	2.48	2.52	255
7	2.06	2.11	2.16	2.21	2.25	2.30	2.35	2.40	2.44	2.49	2.53	257
8	2.06	2.11	2.16	2.21	2.26	2.31	2.36	2.41	2.45	2.50	2.54	260
9	2.07	2.12	2.17	2.22	2.27	2.32	2.37	2.42	2.46	2.51	2.55	262
120	2.08	2.13	2.18	2.23	2.28	2.33	2.38	2.43	2.47	2.52	2.56	264
1	2.09	2.14	2.19	2.24	2.29	2.34	2.39	2.44	2.48	2.53	2.57	266
2	2.09	2.14	2.19	2.24	2.29	2.35	2.40	2.45	2.49	2.54	2.58	268
3	2.10	2.15	2.20	2.25	2.30	2.35	2.40	2.45	2.50	2.55	2.59	271
4	2.11	2.16	2.21	2.26	2.31	2.36	2.41	2.46	2.51	2.56	2.60	273
5	2.12	2.17	2.22	2.27	2.32	2.37	2.42	2.47	2.51	2.56	2.60	275
6	2.12	2.17	2.22	2.27	2.32	2.38	2.43	2.48	2.52	2.57	2.61	277
7	2.13	2.18	2.23	2.28	2.33	2.39	2.44	2.49	2.53	2.58	2.62	279
8	2.14	2.19	2.24	2.29	2.34	2.39	2.44	2.49	2.54	2.59	2.63	282
9	2.14	2.19	2.24	2.29	2.34	2.40	2.45	2.50	2.55	2.60	2.64	284
130	2.15	2.20	2.25	2.30	2.35	2.41	2.46	2.51	2.56	2.61	2.65	286
1	2.16	2.21	2.26	2.31	2.36	2.42	2.47	2.52	2.57	2.62	2.66	288
2	2.16	2.21	2.26	2.32	2.37	2.43	2.48	2.53	2.58	2.63	2.67	290
3	2.17	2.22	2.27	2.32	2.37	2.43	2.48	2.53	2.58	2.63	2.67	293
4	2.18	2.23	2.28	2.33	2.38	2.44	2.49	2.54	2.59	2.64	2.68	295
5	2.19	2.24	2.29	2.34	2.39	2.45	2.50	2.55	2.60	2.65	2.69	297
6	2.19	2.24	2.29	2.35	2.40	2.46	2.51	2.56	2.61	2.66	2.70	299
7	2.20	2.25	2.30	2.36	2.41	2.47	2.52	2.57	2.62	2.67	2.71	301
8	2.21	2.26	2.31	2.36	2.41	2.47	2.52	2.57	2.62	2.67	2.71	304
9	2.21	2.26	2.31	2.37	2.42	2.48	2.53	2.58	2.63	2.68	2.72	306
140	2.22	2.27	2.32	2.38	2.43	2.49	2.54	2.59	2.64	2.69	2.73	308
1	2.23	2.28	2.33	2.39	2.44	2.50	2.55	2.60	2.65	2.70	2.74	310
2	2.23	2.28	2.33	2.39	2.44	2.50	2.55	2.60	2.65	2.70	2.75	312
3	2.24	2.29	2.34	2.40	2.45	2.51	2.56	2.61	2.66	2.71	2.75	315
4	2.24	2.30	2.35	2.41	2.46	2.52	2.57	2.62	2.67	2.72	2.76	317
5	2.25	2.30	2.36	2.42	2.47	2.53	2.58	2.63	2.68	2.73	2.77	319
6	2.26	2.31	2.36	2.42	2.47	2.53	2.58	2.63	2.69	2.73	2.78	321
7	2.26	2.32	2.37	2.43	2.48	2.54	2.59	2.64	2.69	2.74	2.78	323
8	2.27	2.32	2.38	2.44	2.49	2.55	2.60	2.65	2.70	2.75	2.79	326
9	2.27	2.33	2.38	2.44	2.49	2.55	2.60	2.65	2.70	2.75	2.80	328
	59	61	63	65	67	69	71	73	75	77	79	

HEIGHT IN INCHES

Body Surface Area may also be computed accurately, and thus the Normal Consumption of Oxygen obtained with somewhat greater precision. The various steps in the complete computations are shown by the following example:

Male, age 25. Height 145 cm., Weight, 40 kg.

Body-SurfaceArea = 71.84 × *Ht.* 0.725 × *Wt.* 0.425.

Log. 71.84		1.85637
Log. 145	2.16137	
Log. 145 × .725		1.56699
Log. 40	1.60206	
Log. 40 × .425		.68088
Log. Body Surface Area		4.10424

Body Surface Area, 12,710 sq. cm. = 1.271 sq. meters.

This value checks with that in the table.

From the table on page 238 we find that for a male, age 25 years, 37.7 calories of heat is normally produced each hour per square meter of body surface; therefore the heat normally produced by the patient in question would be 37.7 × 1.271 = 47.9 calories per hour. Then from the table on page 237 we find that 47.9 (48.0) calories per hour are equivalent to 166 c.c. of oxygen per minute.

Reading directly from the table on page 242 we find that for a man 145 cm. in height, weighing 40 kg., the normal consumption of oxygen is 164 c. c. per minute — within 1.2 per cent. of the accurately computed values.

Determination of Actual Basal Metabolism.— The preceding pages enable one to determine the normal heat production. The actual heat production may be obtained by direct calorimetry, by determining both the oxygen that is consumed and the carbon dioxid that is exhaled, by determining simply the oxygen that is consumed, or by determining simply the carbon dioxid that is exhaled. When a test of a patient has been made the actual heat production or its equivalent is found and that amount is compared with the normal value, thus to find the metabolic rate.

Before the comparison is made, however, the volume of gas that is observed by a test with the apparatus, must be corrected and brought to standard conditions. These corrections are for temperature, barometer, and water vapor. They may be made in abridged form or carried out to two or three decimal places.

For example, correction for barometer at sea level may ordinarily be omitted and not introduce an error of over 1 per cent., but in full the barometer corrections include those for elevation, the expansion of the brass scale, the density of mercury, capillary depression of the mercury column, pressure of mercury vapor, and latitude. How many of these corrections should be used in the ordinary computations of the metabolic rate?

In the determination of basal metabolic rates the researchist desires the highest degree of accuracy; he wishes to discard no fractions or decimals and to include every possible correction, even tho it be of small value. Such accuracy is positively essential when normal standards are being established, and in laboratories where tests are being made for experimental purposes. The earlier tables in the following section will prove helpful in making these scientifically accurate computations.

For clinical purposes, accuracy in determining the metabolic rate is also essential, but obviously not to so high a degree. Since the metabolic rate is going to be considered in conjunction with other factors in the clinical picture, certain corrections which do not materially alter the final value may be eliminated. Abridgement of the corrections for temperature and barometer is embodied in the method of computations that is shown on page 255.

The temperature of the gas that is in the gasometer of the Open Circuit Method, or in the oxygen bell of the Closed Circuit Method effects the volume of gas that is observed in the test. If the volume be observed at room temperature, as is usual, the corresponding volume under standard conditions — at 32° F. or 0°C. — will be less than the observed volume.

Simplified corrections for temperature may be made by use of the values below. When the gas has the temperature indicated and the volume is read directly, or computed from readings of a linear scale, the corrections shown below are to be made:

Degrees Centigrade	*Correction*
16, 17, 18	Subtract 6 per cent.
19, 20, 21	Subtract 7 per cent.
22, 23, 24, 25	Subtract 8 per cent.

When the volume is read on a special scale that is graduated so that the equivalent volume of gas at 0° C. is read directly from the scale at 19°, 20° or 21° C. the corrections for volumes read at other temperatures are as follows:

Degrees Centigrade	*Correction*
16, 17, 18	Add 1 per cent
19, 20, 21	No correction
22, 23, 24, 25	Subtract 1 per cent

A more complete method of making the corrections for temperature and barometer is given in the following paragrafs:

By Charles' law the volume of a gas at constant pressure is proportional to its absolute temperature which in Fahrenheit is 460° + temperature and in Centigrade is 273° + temperature. Therefore the volume of gas in a gasometer, or in an oxygen bell, can be reduced to a corresponding volume under standard conditions of temperature — 32° F., or 0° C., by the ratio:

$$\frac{273 + 0}{273 + t}$$ when t = temperature in degrees Centigrade.

This ratio may be simplified to

$$\frac{1}{1 + .00367\,t}$$

For 16° C. this ratio becomes .945 and for 32° C., .895; that is, the volume under standard conditions of temperature would be between 95 and 90 per cent. of the observed volume. The correction factor for each degree between 15° C. and 32° C. is given in the following table:

°C.	*Corr. Factor*	*°C.*	*Corr. Factor*	*°C.*	*Corr. Factor*
15	0.95	21	0.93	27	0.91
16	0.94	22	0.92	28	0.91
17	0.94	23	0.92	29	0.90
18	0.94	24	0.92	30	0.90
19	0.93	25	0.92	31	0.90
20	0.93	26	0.91	32	0.90

A variation in temperature of a single degree changes the volume by about one third of 1 per cent. Instead of a separate table, as shown above, it is more convenient to use a combination table that includes corrections for both temperature and barometer as explained in the paragraphs that follow.

An additional correction besides the correction for reduction from an average temperature to 0° Centigrade is needed when changes of temperature have been gradually taking place during the test. That is, if a test has been made with a constant temperature of 20° C. existing thruout the test, only a single correction is necessary, which is the correction that has been explained in the preceding paragrafs, and in certain forms of apparatus not over one degree change in temperature occurs during a test. But when a material change in temperature occurs, amounting to several degrees, in some cases as high as 8 or 10 degrees, a further correction is required.

Benedict found by his tests that it was "justifiable for the sake of simplicity to make an arbitrary correction by adding 1 c. c. of oxygen for each degree Fahrenheit rise in temperature." This is equivalent to 1.8 c. c. for each degree Centigrade and this correction is added, not to the total consumption of oxygen, but to the consumption per minute. Thus if a test be made with temperature at the beginning of 20°C., and at the end of 30°C., the average temperature for which the usual temperature correction would be made is 25°, but in addition a second correction is required on account of the increase in temperature from 20° to 30°. For this increase of 10°, 10 times 1.8 or 18 c. c. would be added to the actual consumption of oxygen per minute.

Barometric Pressure also affects the volume of the gas that is observed in the test. If the volume is observed when there is a low atmospheric pressure — a barometric reading of 29 inches or 737 millimeters, for example — the volume when exprest under standard conditions (pressure of 760 millimeters) will be smaller than the volume which was originally observed.

A simplified method of correcting the volume for barometric pressure is by use of the values below:

Approximately, for each 10 mm. below 760, subtract 1 per cent.
for each 10 mm. above 760, add 1 per cent.
(These corrections will not hold true for wide ranges.)

Accurate corrections may be determined by the following method: According to Boyle's law the volume of gas at constant temperature is diminished in the same ratio as the pressure upon it is increased; that is, the volume varies inversely as the pressure or

$$pv = PV \text{ when } t \text{ is constant}$$

$$V = \frac{pv}{P} \qquad \frac{V}{v} = \frac{p}{P} = \frac{p}{760}$$

$$\therefore V = \frac{p}{760} v$$

or, corrected volume = observed volume multiplied by

$$\frac{\text{barometer in millimeters}}{760}$$

At 700 mm. the ratio $\frac{p}{760}$ becomes .92 and at 780, 1.03; that is the volume under standard conditions of pressure would be 92 per cent. of the observed volume if the test be made at 700 mm. and it would become 103 per cent. if the test be made at 780 mm. A single millimeter change in pressure would change the volume one seventh of 1 per cent.

In the above formula 'p' is the true barometric pressure in millimeters of murcury as would be obtained directly from an aneroid barometer or as obtained by correcting the reading of a mercurial barometer for the expansion of mercury and of the brass scale. (See table on next page).

To correct the readings of a mercurial barometer for expansion of the brass scale (which is minus) and the expansion of the mercury (which is plus) subtract the millimeter and tenths of millimeter given in the table from the scale readings that are taken from the barometer thus to obtain the corrected reading of the barometer.

By combining the foregoing corrections, one for temperature and the other for barometric pressure, a single table for temperature-barometer correction may be prepared, similar to the table on page 256. This table, however, is for saturated gases. By modifying the results obtained from this table in accordance with the values on page 258, the corresponding volume for dry gases may be obtained.

The combined effect of temperature and barometer may be embodied in one table; such a table may be prepared for a so-called saturated gas or for a dry gas.

CORRECTIONS IN MILLIMETERS OF BAROMETER READINGS FOR EXPANSION OF BRASS SCALE AND MERCURY COLUMN.

These Corrections are necessary in Accurate Computations.

BAROMETER READINGS IN MILLIMETERS

	700	710	720	730	740	750	760	770	780	
16	1.8	1.9	1.9	1.9	1.9	2.0	2.0	2.0	2.0	61
17	1.9	2.0	2.0	2.0	2.1	2.1	2.1	2.1	2.2	63
18	2.1	2.1	2.1	2.1	2.2	2.2	2.2	2.3	2.3	64
19	2.2	2.2	2.2	2.3	2.3	2.3	2.4	2.4	2.4	66
20	2.3	2 3	2.3	2.4	2.4	2.4	2.5	2.5	2.5	68
21	2.4	2.4	2.5	2.5	2.5	2.6	2.6	2.6	2.7	70
22	2.5	2.5	2.6	2.6	2.7	2.7	2.7	2.8	2.8	72
23	2.6	2.7	2.7	2.7	2.8	2.8	2.9	2.9	2.9	73
24	2.7	2.8	2.8	2.9	2.9	2.9	3.0	3.0	3.1	75
25	2.9	2.9	2.9	3.0	3.0	3.1	3.1	3.1	3.2	77
26	3.0	3.0	3.1	3.1	3.1	3.2	3.2	3.3	3.3	79
27	3.1	3.1	3.2	3.2	3.3	3.3	3.3	3.4	3.4	81
28	3.2	3.2	3 3	3.3	3.4	3.4	3.5	3.5	3.6	82
29	3.3	3.4	3.4	3.5	3.5	3.5	3.6	3.6	3.9	84
30	3.4	3.5	3.5	3.6	3.6	3.7	3.7	3.8	3.8	86
31	3.5	3.6	3.6	3.7	3.7	3 8	3.8	3.9	3.9	88
32	3.6	3.7	3.8	3.8	3.9	3.9	4.0	4.0	4.1	90
	27.6	27.9	28 3	28.7	29.1	29.5	29.9	30.3	30.7	

Barometer in Inches

A gas, like air or oxygen, that is used in metabolism apparatus, is considered as dry if it contains less than 1 per cent. of saturation; but if it contains water vapor to a greater extent it may be regarded as saturated.

In the Open Circuit Method the exhaled air is inclosed within a spirometer or a gasometer and exposed to a free water surface and is, therefore, saturated. In the Closed Circuit Method, soda lime or its equivalent removes carbon dioxid and at the same time removes practically all the water vapor. Benedict states that it has been shown by means of a sensitive psychrometer placed in the air circuit of a closed circuit apparatus, that the percentage of moisture is so small that in practice it may be neglected in the calculation of the oxygen consumption during short periods.

The volume of a perfect gas varies inversely with the pressure, or $\frac{V}{v} = \frac{p}{P} = \frac{p}{760}$. To make this ratio suitable for saturated gases it is necessary to subtract from p, the true barometric pressure, the amount of that pressure which is caused by water vapor (e). This makes the ratio $\frac{p-e}{760}$ which reduces a saturated gas to standard conditions of pressure, 760 mm., and dryness.

The Open Circuit Method has a saturated gas. Volumes of gas that are observed when making tests by the Open Circuit Method must be corrected for the combined effects of temperature, barometric pressure, and saturation. This correction is made by multiplying the observed volume by the correction factor

$$\frac{1}{1 + .00367\,t} \times \frac{p-e}{760}$$

Logarithms of this factor are given in the table on pages 257.

The table is used for reducing a volume of gas that is saturated with water vapor and which is at a temperature of 16° to 31°C. and under a pressure equal to a barometric height of 700 to 780 millimeters of mercury, to an equivalent volume of gas that is dry and under standard conditions of temperature, 0°C., and a barometric pressure of 760 millimeters. The table includes corrections for water vapor, the expansion of mercury and of the brass scale of the barometer. The temperature of the gas inside the spirometer, or gasometer, is assumed to be the same as the temperature of the barometer.

To use the table, enter with the barometric reading as taken from a mercurial barometer and with temperature exprest in Centigrade degrees. If, however, the aneroid reading is used, an error of 1 to 4 mm. or one seventh to one half of 1 per cent. will result.

This table for reducing a gas that is saturated with water vapor is the one to be used for open circuit metabolism apparatus like the Tissot or the gasometer, or with the gas analysis method of determining metabolism.

Accurate computations from the formula for correcting the observed volume for temperature and barometer give the following result:

Observed Volume, 250 c. c., Barometric Pressure, 740 mm. Temperature, 20° C., dry.

$$\frac{250 \times 273}{273+t} \times \frac{p}{760} = 250 \times \frac{273}{293} \times \frac{740}{760} = 226.8 \text{ c.c.} = \text{corrected volume.}$$

Simplified computations using approximate corrections for temperature and barometer give the following value:

Temperature Correction

Temperature Degrees Cent.	*Correction to 0° Centigrade*
16, 17, 18	Subtract 6 %
19, 20, 21	" 7 %
22, 23, 24, 25	" 8 %

Barometer Correction

Corrected volume $= \frac{p}{760} \times$ observed volume, or approximately

For each 10 mm. below 760 subtract 1%
For each 10 mm. above 760 add 1%

Observed Volume, 250 c. c., Barometric Pressure, 740 mm., Temperature 20° C., dry.

$$250 \times .93 \times \frac{740}{760} = 226.4 \text{ c. c.}$$

$$\text{or, } 250 \times .93 \times .98 = 227.9 \text{ c. c.}$$

Computations from the table for the reduction of the volume of saturated gas on pages 256 and 257 and the table of corrections for dry gas on page 258 give the results below.

Observed Volume, 250 c. c., Barometric Pressure, 740 mm., Temperature, 20° C., dry.

Log. of observed Volume	2.3979
Log. factor for 20°, 740 mm.	$\bar{1}.9459$
Correction for dry gas 2.4%	
Log. 1.024	.0103
Log. corrected Volume	2.3541
Corrected Volume	226.0c.c.

For ordinary cases the three simplified methods given above show results within 1 per cent. of the result obtained by the formula.

LOGARITHMIC TABLE FOR REDUCING VOLUMES OF SATURATED GAS TO STANDARD CONDITIONS

For Use with Open Circuit Method

TEMPERATURE CENTIGRADE

BAROMETER IN MILLIMETERS	16	17	18	19	20	21	22	23	BAROMETER IN INCHES
700	$\bar{1}$.9298	9277	9255	9233	9211	9188	9164	9141	27.6
702	9310	9289	9267	9245	9223	9200	9177	9153	27.7
704	9323	9302	9279	9257	9236	9212	9189	9166	27.7
706	9335	9314	9292	9270	9248	9225	9202	9179	27.8
708	9348	9327	9305	9283	9260	9237	9214	9192	27.8
710	9361	9340	9318	9296	9273	9251	9228	9205	27.9
712	9373	9352	9330	9308	9285	9263	9240	9217	28.0
714	9385	9364	9342	9320	9298	9275	9252	9229	28.1
716	9398	9377	9355	9333	9311	9288	9265	9242	28.1
718	9410	9389	9367	9345	9323	9300	9277	9254	28.2
720	9423	9402	9380	9358	9336	9313	9290	9267	28.3
722	9435	9414	9392	9370	9348	9325	9302	9279	28.4
724	9447	9426	9404	9382	9360	9337	9314	9291	28.5
726	9460	9439	9416	9394	9373	9350	9327	9304	28.5
728	9472	9451	9428	9406	9385	9362	9339	9316	28.6
730	9484	9463	9441	9419	9398	9375	9352	9329	28.7
732	9496	9475	9453	9431	9410	9387	9364	9341	28.8
734	9508	9487	9465	9443	9422	9399	9376	9353	28.9
736	9520	9499	9478	9456	9434	9411	9388	9365	28.9
738	9532	9511	9490	9468	9446	9423	9400	9377	29.0
740	9544	9523	9502	9480	9459	9436	9413	9390	29.1
742	9556	9535	9514	9492	9471	9448	9425	9402	29.2
744	9569	9547	9526	9504	9483	9460	9437	9414	29.3
746	9580	9559	9537	9516	9494	9472	9449	9426	29.3
748	9592	9571	9549	9528	9506	9483	9461	9438	29.4
750	9603	9583	9561	9540	9518	9495	9473	9450	29.5
752	9615	9594	9573	9551	9530	9507	9485	9462	29.6
754	9627	9606	9585	9563	9541	9519	9497	9474	29.7
756	9639	9618	9596	9575	9553	9531	9509	9486	29.7
758	9651	9630	9608	9587	9565	9542	9521	9498	29.8
760	9662	9641	9620	9598	9577	9554	9532	9509	29.9
762	9674	9653	9632	9610	9588	9566	9544	9521	30.0
764	9685	9665	9643	9621	9600	9578	9556	9532	30.1
766	9697	9676	9655	9633	9612	9589	9568	9544	30.1
768	9709	9688	9666	9645	9623	9601	9579	9556	30.2
770	9720	9699	9677	9656	9635	9613	9590	9567	30.3
772	9732	9711	9689	9668	9646	9624	9602	9579	30.4
774	9743	9722	9700	9679	9658	9636	9613	9591	30.5
776	9755	9734	9712	9691	9670	9647	9625	9602	30.5
778	9766	9745	9723	9702	9681	9658	9636	9614	30.6
780	9777	9756	9735	9714	9692	9670	9648	9625	30.7
	61	63	64	66	68	70	72	73	

TEMPERATURE, FAHRENHEIT

LOGARITHMIC TABLE FOR REDUCING VOLUMES OF SATURATED GAS TO STANDARD CONDITIONS

For Full Explanation of Table See Page 254

TEMPERATURE, CENTIGRADE

BAROMETER IN MILLIMETERS

	24	25	26	27	28	29	30	31	
700	$\bar{1}$.9117	9093	9068	9044	9017	8991	8964	8937	27.6
702	9129	9105	9080	9056	9029	9003	8976	8949	27.7
704	9142	9118	9093	9069	9042	9016	8989	8962	27.7
706	9155	9131	9106	9082	9055	9029	9002	8975	27.8
708	9167	9143	9118	9094	9067	9041	9014	8987	27.8
710	9181	9157	9132	9108	9081	9055	9027	9001	27.9
712	9193	9169	9144	9120	9093	9067	9040	9015	28.0
714	9206	9181	9157	9133	9106	9080	9054	9027	28.1
716	9218	9194	9170	9146	9119	9093	9067	9040	28.1
718	9230	9206	9182	9158	9131	9105	9080	9052	28.2
720	9244	9220	9195	9171	9145	9119	9093	9066	28.3
722	9256	9232	9207	9183	9157	9131	9105	9078	28.4
724	9268	9244	9219	9195	9170	9144	9117	9090	28.5
726	9280	9256	9232	9208	9183	9157	9130	9103	28.5
728	9292	9268	9244	9220	9195	9169	9142	9115	28.6
730	9305	9281	9257	9233	9208	9182	9155	9128	28.7
732	9317	9293	9269	9245	9220	9194	9167	9140	28.8
734	9329	9305	9281	9257	9232	9206	9180	9153	28.9
736	9342	9318	9294	9270	9244	9218	9192	9166	28.9
738	9354	9330	9306	9282	9256	9230	9204	9178	29.0
740	9367	9343	9318	9294	9268	9243	9216	9190	29.1
742	9379	9354	9330	9306	9280	9255	9228	9202	29.2
744	9391	9366	9342	9318	9292	9267	9241	9214	29.3
746	9403	9379	9355	9331	9305	9280	9254	9227	29.3
748	9415	9391	9367	9343	9317	9292	9266	9239	29.4
750	9427	9403	9379	9355	9330	9304	9278	9251	29.5
752	9439	9415	9391	9367	9342	9316	9290	9263	29.6
754	9451	9427	9403	9379	9354	9328	9303	9275	29.7
756	9462	9439	9415	9391	9366	9340	9315	9288	29.7
758	9474	9450	9427	9403	9377	9352	9327	9300	29.8
760	9486	9462	9439	9415	9389	9364	9339	9312	29.9
762	9498	9474	9451	9427	9401	9376	9351	9324	30.0
764	9599	9486	9463	9438	9413	9388	9363	9336	30.1
766	9521	9498	9474	9450	9425	9400	9375	9348	30.1
768	9533	9509	9485	9462	9436	9411	9386	9360	30.2
770	9545	9521	9497	9473	9448	9423	9398	9372	30.3
772	9556	9533	9509	9485	9460	9435	9409	9384	30.4
774	9568	9545	9521	9497	9472	9446	9421	9396	30.5
776	9579	9556	9532	9508	9483	9458	9433	9407	30.5
778	9591	9567	9544	9520	9495	9470	9445	9419	30.6
780	9602	9579	9555	9532	9506	9481	9456	9430	30.7
	75	77	79	81	82	84	86	88	

BAROMETER IN INCHES

TEMPERATURE, FAHRENHEIT

The Closed Circuit Method has a gas that is considered dry. Volumes of gas that are observed when making tests by the Closed Circuit Method may be corrected for temperature and barometric pressure by the following procedure:

Make computations for gas as if it were saturated and add the small correction found in the table below, which covers temperatures from 16° to 31°C. and barometric heights of from 700 to 780 mm. of mercury.

TABLE FOR REDUCING VOLUME OF DRY GAS TO BE USED IN CONJUNCTION WITH THE PRECEDING LOGARITHMIC TABLE FOR SATURATED GAS

Percentage Factors to be added to Saturated Volume thus to Correct for Dry Gas.

TEMPERATURE CENTIGRADE	Barometer in Millimeters									TEMPERATURE FAHRENHEIT
	700	710	720	730	740	750	760	770	780	a
16	2.0	2.0	1.9	1.9	1.9	1.9	1.8	1.8	1.8	61
19	2.1	2.1	2.1	2.0	2.0	2.0	1.9	1.9	1.8	63
18	2.3	2.2	2.2	2.2	2.1	2.1	2.1	2.1	2.0	64
19	2.4	2.4	2.3	2.3	2 3	2.2	2.2	2.2	2.2	66
20	2.6	2.5	2.5	2.4	2.4	2.4	2.4	2.3	2.3	68
21	2.7	2.7	2.7	2.6	2.6	2.6	2.5	2.5	2.5	70
22	2.9	2.9	2.8	2.8	2.8	2.7	2.7	2.7	2.6	72
23	3.1	3.1	3.0	3.0	2.9	2.9	2.9	2.8	2.8	73
24	3.3	3.3	3.2	3.2	3.1	3.1	3.0	3.0	3.0	75
25	3.5	3.5	3.4	3.4	3.4	3.3	3.2	3.2	3.1	77
26	3.7	3.7	3.6	3.6	3.5	3.5	3.4	3.4	3.3	79
27	4.0	3.9	3.9	3.8	3.8	3.7	3.7	3.6	3.6	81
28	4 2	4.2	4.1	4.1	4.0	3.9	3.9	3.8	3.8	82
29	4.5	4.4	4.4	4.3	4.2	4.2	4.1	4.1	4.0	84
30	4.7	4.6	4.6	4.5	4.5	4.4	4.4	4.3	4.3	86
31	5.0	5.0	4.9	4.8	4.8	4.7	4.6	4.6	4.5	88
	27.6	27.9	28.3	28.7	29.1	29.5	29.9	30.3	30.7	
	Barometer in Inches									

The Respiratory Quotient, that is, the ratio of the volume of carbon dioxid that is exhaled to the volume of oxygen that is consumed, should be determined for each test when for special reasons it is desired to obtain precise values of the basal metabolic rate. Various values of the respiratory quotient and the corresponding calorific values for one liter of oxygen are given in the table below. The values that are commonly used as average values are printed in heavy face type,— respiratory quotient of 0.82 and corrresponding calorific value 4 83.

THE CALORIFIC VALUES OF ONE LITER OF OXYGEN FOR NON-PROTEIN RESPIRATORY QUOTIENTS ARE GIVEN IN THE TABLE BELOW

(From Zuntz and Schumburg Physiologie des Marches Berlin 1901)

R. Q.	*Cals.*	*R. Q.*	*Cals.*	*R. Q.*	*Cals.*
0.71	4.69	0.81	4.81	0.91	4.94
.72	4.70	.82	4.83	.92	4.95
.73	4.71	.83	4.84	.93	4.96
.74	4.73	.84	4.85	.94	4.97
.75	4.74	.85	4.86	.95	4.99
.76	4.75	.86	4.88	.96	5.00
.77	4.76	.87	4.89	.97	5.01
.78	4.78	.88	4.90	.98	5.02
.79	4.79	.89	4.91	.99	5.03
.80	4.80	.90	4.92	1.00	5.05

In the Gas Analysis Method the actual basal metabolism is determined by the following procedure: Obtain the volume of expired air by test of patient as described in chapters 4 an 5. Correct for temperature, barometer and saturation of gas as explained in preceding pages of this chapter.

Find the percentage of carbon dioxid by analyzing samples of the expired air as explained in chapters 4 and 5; then subtract the percentage of carbon dioxid in pure outside air (which is taken as 0.03 or 0.04 per cent.); multiply this percentage by the corrected volume per minute of expired air.

Find the percentage of oxygen in the expired air by the methods referred to in chapters 4 and 5, and explained more fully in Haldane's "Methods of Air Analysis". To compute the volume of oxygen even after knowing the percentage in the sample requires the consideration of several related facts. The percentage of oxygen in pure outside air is generally taken as 20.93; and combining with this 0.04 per cent. for carbon dioxid gives 79.03 per cent. for nitrogen. Now the volume of dry air has diminished in the process of respiration because the volume of oxygen that has been taken up is greater than the volume of carbon dioxid that has been given off. Therefore, since nitrogen is neither taken up nor given off during respiration, it is evident that for every 100 volumes of air that is expired there are not 20.93 volumes of oxygen as in pure outside air, but a volume of

$$\frac{20.93 \times \text{Per cent. of nitrogen in sample}}{79.03}$$

Subtract from the above volume the volume that would be indicated by the analysis of the samples of expired air to find the true volume of oxygen consumption.

OBSERVATION AND COMPUTATION SHEET FOR GAS ANALYSIS METHOD

Form of data sheet that is used at the New York Post Graduate Medical School and Hospital. A similar form is also used at the Mayo Clinic (see form in Boston Med. and Surg. Jour., Sept., 1921.)

METABOLISM LABORATORY

Case No. 9569.
Lab. No. 27110.
Name Rose Fraser Age 22.

Date June 17 1921
Gasom. No. 1
Samp. Bottle No. 4, 5 & 6

Barometer 752.6 mm.	Log. Fact. Gasom.	97313
Temp. Gasom. 23 °C.	Log. Gasom. diff.	95231
	Log. Fact. S. T. P. D.	9523
	Log. Total vent. (add)	87774
Gasom. End 89.9 cm.	Log. Time	02119
Gasom. Start 0.3 cm.	Log. Vent. per min. (sub.)	85655 = 7.19 L.
Gasom. Diff. 89.6 cm.	Log. % O_2 absorbed	63548
	Log. O_2 absorbed (add)	49203 = 310.5 cc.
Duration of test 10 m. 30 s. = 10.5 min.	Log. Cal. value O_2 + log. 60	4551
	Log. Total Cal. per hr. (add)	94713 = 88.54 Cal.
	Log. Surface Area	15229
CO_2 Expired 3.31%	Log. Cal. per sq. m. hr. (sub.)	79484 = 62.35 Cal.
CO_2 Inspired 0.04%		
CO_2 Produced (sub.) 3.27%		
	Cal. per sq. m. hr. (above nor.)	62.35
O_2 Inspired 21.15%	Cal. per sq. m. hr. normal	37
O_2 Expired 16.83%	Cal. per sq. m. hr. (below nor.)	
O_2 Absorbed (sub.) 4.32%	Difference (sub.)	25.35
	Log. difference	4039
Log. % CO_2 produced 51455	Log. normal	5682
Log. % O_2 absorbed 63548	Log. B. M. % (sub.)	8357
Log. Resp. Quot. (sub.) 87907 = 0.76		

BASAL METABOLISM +68%

Gas Analysis By J.S.J. Haldane No. 4	Gas Analysis By J.S.J. Haldane No. 5
9.780 − .002 = 9.778	9.555 + 0 = 9.555
9.455 − .001 = 9.454	9.235 + .004 = 9.239
.324	.316
7.810 + .001 = 7.811	7.625 + .003 = 7.628
1.643	1.611

Log. CO_2 diff.	51055	Log. O_2 diff.	21564	Log. CO_2 diff.	49969	Log. O_2 diff.	20710
Log. sample	99025	Log. sample	99025	Log. sample	98023	Log. sample	98023
Log. CO_2 %	52030	Log. O_2 %	22539	Log. CO_2 %	51946	Log. O_2 %	22687
CO_2 %	3.31	O_2 %	16.8	CO_2 %	3.30	O_2 %	16.86

Notes:
Ht., 153 cm.
Wt., 104 lbs.
Surface Area, 1.42 Sq. M.
Resp. 22
Pulse 128, 130

Avg. CO_2 3.31%
Avg. O_2 16.83%
CO_2 + O_2 20.14%

Readings by: J.S.J.
Checked by: C.V.B.
Calculations by: J.S.J.
First check by: C.V.B.
Second check by: W.E.H.

OBSERVATION AND COMPUTATION SHEETS
For Closed Circuit Method

A convenient form (prepared by Editor) for recording observations and computations by the Closed Circuit Method is shown on the following pages.

BASAL METABOLISM

Name of Patient ....

Test No. .... Date ....

Diagnosis before test ....

....

Local Physician ....

Technician for test ....

Make of Apparatus:

Result of test: Unusually good, accepted, rejected.
(Underline)

BASAL METABOLIC RATE
As determined by test ....

To Find the Patient's Actual Consumption of Oxygen

Barometer............inches equals ....millimeters
(Multiply by 25.4)

Thermometer (Temperature in apparatus)

Beginning of Test. C

Time

Start	....h....m....s	....	....
End	....h....m....s	....	....
Duration	....mins	....	....

Volume of Oxygen

Start	........cc.	....	....
End	........cc.	....	....
Consumption of Oxygen	........cc.	....	....
Per minute	........cc.	....	....
Average			........cc.

Thermometer

End of Test C

Average beginning and end of Test C

Correction for Temperature (Page 264) ....cc.

Correction for Barometer (Page 264) ....cc.

Patient's actual consumption of oxygen per minute, corrected to temperature of 0 degrees C. and barometer pressure of 760 mm.

To Find the Patient's Normal Consumption of Oxygen

Age........years. Male, Female
(Underline)

Weight (without clothing).......pounds or.......kilograms

Height (without shoes)........inches or........centimeters

Normal Consumption of Oxygen

For weight and height noted, ages 20 to 50 years (P. 242) ......cc.

Correction for other ages (Page 241) ......cc.

Correction for females (Page 241) ......cc.

Patient's Normal Consumption ......cc.

Patient's Actual Consumption as found by tests ......cc.

Consumption above normal (plus), below (minus) ......cc.
(Underline)

Per cent. above normal (plus), below (minus) ....
(Divide the plus or minus cc. by normal)

BASAL METABOLIC RATE ....

(The percentage of oxygen consumed above or below normal is the plus or minus basal metabolic rate.)

Observations Auxiliary to Test, that may be Recorded as a Guide in Interpreting Results

Pulse Rate (taken during, or at beginning and end of test) . . . .

Respiration (taken during test) . . . .

Blood Pressure (taken after test) . . . . . . Systolic . . . . . . Diastolic

Buccal Temperature (taken after test) . . . .

Temperature Corrections for Readings of Oxygen Scale.

Degrees Centigrade	Ordinary Scale	Special Scale
16, 17, 18	Subtract 6%	add 1%
19, 20, 21	" 7%	no correction
22, 23, 24, 25	" 8%	subtract 1%

Barometer Corrections for Readings of Oxygen Scale

The correction for barometer pressure is found by the following formula:

$$\text{Consumption of oxygen multiplied by } \frac{\text{bar pressure in mm.}}{760}$$

or approximately:

For each 10 mm. below 760 subtract 1 per cent.

For each 10 mm. above 760 add 1 per cent.

COMPUTATION SHEET

BENEDICT UNIVERSAL APPARATUS

From page 103

J. D., Age 49 Ht., 185 cm. Wt., 67.2 kg. August 21, 1921

"A" Ward

Period I	Time 9.2	Period II	Time 9.87	Period III	Time 8.02
R 7160	T 21	R 7050	T 21	R 7050	T 22
R 3180	T 21	R 2700	T 22	R 3350	T 22
3980	21	4350	21.5	3700	22

	No.	*Log.*
Urine Collected	9.10 to 11.08	
Total time of periods	27.09	1.4328
Period of Urine Collection	118.	2.0719
		$\bar{1}$.3609
Total N of Collected Urine	1.4	0.1461
Urinary N for time of period	.32	$\bar{1}$.5070
Total Readings	12030	4.0802
Vol. reduced to 0°C.		
273 ÷ (t + 273)		$\bar{1}$.9672
Vol. reduced to 760 mm.		
(Bar. ÷ 760)		$\bar{1}$.9983
Corrected Vol. O_2	11110	4.0457
C. C. per liter	1000	3.
Liters O_2 consumed	11.110	1.0457
Vol. 1 gm. O_2	0.699	$\bar{1}$.8445
Wt. O_2 consumed	15.90	1.2012
Urinary N	.32	$\bar{1}$.5070
O_2 per gm. Ur. N	8.45	0.9269
O_2 for Protein	2.716	0.4339
Wt. O_2 Consumed	15.90	
Wt. O_2 for Protein	2.716	
Wt. N. P. O_2	13.184	1.1199
Vol. 1 gm. O_2	0.699	$\bar{1}$.8445
Vol. N. P. O_2	9.212	0.9644

Wt. Soda Lime and Acid (2)	4415.42
Wt. Soda Lime and Acid (1)	4398.15
Wt. CO_2 Expired	17.27

	No.	*Log.*
Urinary N	.32	$\bar{1}$.5070
CO_2 per gm. Ur. N.	9.35	0.9708
CO_2 for Protein	3.004	0.4778
Wt. CO_2 Expired	17.27	
Wt. CO_2 for Protein	3.004	
Wt. N. P. CO_2	14.266	1.1544
Vol. 1 gm. CO_2	0.5087	$\bar{1}$.7065
Vol. N. P. CO_2	7.259	0.8609
Vol. N. P. O_2	9.212	0.9644
N. P. R. Q.	.7879	$\bar{1}$.8965

Liters O_2 Consumed	11.11	1.0457
Duration of Periods	27.09	1.4328
O_2 Consumed per min.	.4102	$\bar{1}$.6129
Min. per day	1440	3.1584
Cal. per Liter O_2	4.789	.6802
Cal. per 24 hrs.	2828	3.4515
Theoretical	1586	3.2004
Basal Metabolism	1.778	.2511
Change to %	100	
	177.8%	

LOGARITHMS OF NUMBERS FROM 1.000 TO 1.499

·	0	1	2	3	4	5	6	7	8	9
1.00	0.0000	0004	0009	0013	0017	0022	0026	0030	0035	0039
1.01	0043	0048	0052	0056	0060	0065	0069	0073	0077	0082
1.02	0086	0090	0095	0099	0103	0107	0111	0116	0120	0124
1.03	0128	0133	0137	0141	0145	0149	0154	0158	0162	0166
1.04	0170	0175	0179	0183	0187	0191	0195	0199	0204	0208
1.05	0212	0216	0220	0224	0228	0233	0237	0241	0245	0249
1.06	0253	0257	0261	0265	0269	0273	0278	0282	0286	0290
1.07	0294	0298	0302	0306	0310	0314	0318	0322	0326	0330
1.08	0334	0338	0342	0346	0350	0354	0358	0362	0366	0370
1.09	0374	0378	0382	0386	0390	0394	0398	0402	0406	0410
1.10	0.0414	0418	0422	0426	0430	0434	0438	0441	0445	0449
1.11	0453	0457	0461	0465	0469	0473	0477	0481	0484	0488
1.12	0492	0496	0500	0504	0508	0512	0515	0519	0523	0527
1.13	0531	0535	0538	0542	0546	0550	0554	0558	0561	0565
1.14	0569	0573	0577	0580	0584	0588	0592	0596	0599	0603
1.15	0607	0611	0615	0618	0622	0626	0630	0633	0637	0641
1.16	0645	0648	0652	0656	0660	0663	0667	0671	0674	0678
1.17	0682	0686	0689	0693	0697	0700	0704	0708	0711	0715
1.18	0719	0722	0726	0730	0734	0737	0741	0745	0748	0752
1.19	0755	0759	0763	0766	0770	0774	0777	0781	0785	0788
1.20	0.0792	0795	0799	0803	0806	0810	0813	0817	0821	0824
1.21	0828	0831	0835	0839	0842	0846	0849	0853	0856	0860
1.22	0864	0867	0871	0874	0878	0881	0885	0888	0892	0896
1.23	0899	0903	0906	0910	0913	0917	0920	0924	0927	0931
1.24	0934	0938	0941	0945	0948	0952	0955	0959	0962	0966
1.25	0969	0973	0976	0980	0983	0986	0990	0993	0997	1000
1.26	1004	1007	1011	1014	1017	1021	1024	1028	1031	1035
1.27	1038	1041	1045	1048	1052	1055	1059	1062	1065	1069
1.28	1072	1075	1079	1082	1086	1089	1092	1096	1099	1103
1.29	1106	1109	1113	1116	1119	1123	1126	1129	1133	1136
1.30	0.1139	1143	1146	1149	1153	1156	1159	1163	1166	1169
1.31	1173	1176	1179	1183	1186	1189	1193	1196	1199	1202
1.32	1206	1209	1212	1216	1219	1222	1225	1229	1232	1235
1.33	1239	1242	1245	1248	1252	1255	1258	1261	1265	1268
1.34	1271	1274	1278	1281	1284	1287	1290	1294	1297	1300
1.35	1303	1307	1310	1313	1316	1319	1323	1326	1329	1332
1.36	1335	1339	1342	1345	1348	1351	1355	1358	1361	1364
1.37	1367	1370	1374	1377	1380	1383	1386	1389	1392	1396
1.38	1399	1402	1405	1408	1411	1414	1418	1421	1424	1427
1.39	1430	1433	1436	1440	1443	1446	1449	1452	1455	1458
1.40	0.1461	1464	1467	1471	1474	1477	1480	1483	1486	1489
1.41	1492	1495	1498	1501	1504	1508	1511	1514	1517	1520
1.42	1523	1526	1529	1532	1535	1538	1541	1544	1547	1550
1.43	1553	1556	1559	1562	1565	1569	1572	1575	1578	1581
1.44	1584	1587	1590	1593	1596	1599	1602	1605	1608	1611
1.45	1614	1617	1620	1623	1626	1629	1632	1635	1638	1641
1.46	1644	1647	1649	1652	1655	1658	1661	1664	1667	1670
1.47	1673	1676	1679	1682	1685	1688	1691	1694	1697	1700
1.48	1703	1706	1708	1711	1714	1717	1720	1723	1726	1729
1.49	1732	1735	1738	1741	1744	1746	1749	1752	1755	1758

LOGARITHMS OF NUMBERS FROM 1,500 TO 1,999

	0	1	2	3	4	5	6	7	8	9
1.50	0.1761	1764	1767	1770	1772	1775	1778	1781	1784	1787
1.51	1790	1773	1796	1798	1801	1804	1807	1810	1813	1816
1.52	1818	1821	1824	1827	1830	1833	1836	1838	1841	1844
1.53	1847	1850	1853	1855	1858	1861	1864	1867	1870	1872
1.54	1875	1878	1881	1884	1886	1889	1892	1895	1898	1901
1.55	1903	1906	1909	1912	1915	1917	1920	1923	1926	1928
1.56	1931	1934	1937	1940	1942	1945	1948	1951	1953	1956
1.57	1959	1962	1965	1967	1970	1973	1976	1978	1981	1984
1.58	1987	1989	1992	1995	1998	2000	2003	2006	2009	2011
1.59	2014	2017	2019	2022	2025	2028	2030	2033	2036	2038
1.60	0.2041	2044	2047	2049	2052	2055	2057	2060	2063	2066
1.61	2068	2071	2074	2076	2079	2082	2084	2087	2090	2092
1.62	2095	2098	2101	2103	2106	2109	2111	2114	2117	2119
1.63	2122	2125	2127	2130	2133	2135	2138	2140	2143	2146
1.64	2148	2151	2154	2156	2159	2162	2164	2167	2170	2172
1.65	2175	2177	2180	2183	2185	2188	2191	2193	2196	2198
1.66	2201	2204	2206	2209	2212	2214	2217	2219	2222	2225
1.67	2227	2230	2232	2235	2238	2240	2243	2245	2248	2251
1.68	2253	2256	2258	2261	2263	2266	2269	2271	2274	2276
1.69	2279	2281	2284	2287	2289	2292	2294	2297	2299	2302
1.70	0.2304	2307	2310	2312	2315	2317	2320	2322	2325	2327
1.71	2330	2333	2335	2338	2340	2343	2345	2348	2350	2353
1.72	2355	2358	2360	2363	2365	2368	2370	2373	2375	2378
1.73	2380	2383	2385	2388	2390	2393	2395	2398	2400	2403
1.74	2405	2408	2410	2413	2415	2418	2420	2423	2425	2428
1.75	2430	2433	2435	2438	2440	2443	2445	2448	2450	2453
1.76	2455	2458	2460	2463	2465	2467	2470	2472	2475	2477
1.77	2480	2482	2485	2487	2490	2492	2494	2497	2499	2502
1.78	2504	2507	2509	2512	2514	2516	2519	2521	2524	2526
1.79	2529	2531	2533	2536	2538	2541	2543	2545	2548	2550
1.80	0.2553	2555	2558	2560	2562	2565	2567	2570	2572	2574
1.81	2577	2579	2582	2584	2586	2589	2591	2594	2596	2598
1.82	2601	2603	2605	2608	2610	2613	2615	2617	2620	2622
1.83	2625	2627	2629	2632	2634	2636	2639	2641	2643	2646
1.84	2648	2651	2653	2655	2658	2660	2662	2665	2667	2669
1.85	2672	2674	2676	2679	2681	2683	2686	2688	2690	2693
1.86	2695	2697	2700	2702	2704	2707	2709	2711	2714	2716
1.87	2718	2721	2723	2725	2728	2730	2732	2735	2737	2739
1.88	2742	2744	2746	2749	2751	2753	2755	2758	2760	2762
1.89	2765	2767	2769	2772	2774	2776	2778	2781	2783	2785
1.90	0.2788	2790	2792	2794	2797	2799	2801	2804	2806	2808
1.91	2810	2813	2815	2817	2819	2822	2824	2826	2828	2831
1.92	2833	2835	2838	2840	2842	2844	2847	2849	2851	2853
1.93	2856	2858	2860	2862	2865	2867	2869	2871	2874	2876
1.94	2878	2880	2882	2885	2887	2889	2891	2894	2896	2898
1.95	2900	2903	2905	2907	2909	2911	2914	2916	2918	2920
1.96	2923	2925	2927	2929	2931	2934	2936	2938	2940	2942
1.97	2945	2947	2949	2951	2953	2956	2958	2960	2962	2964
1.98	2967	2969	2971	2973	2975	2978	2980	2982	2984	2986
1.99	2989	2991	2993	2995	2997	2999	3002	3004	3006	3008

LOGARITHMS OF NUMBERS FROM 2.00 TO 5.99 AND BY INTERPOLATION FROM 2.000 TO 5.999

	0	1	2	3	4	5	6	7	8	9	Interpolation 1	2	3	4	5
2.0	0.3010	3032	3054	3075	3096	3118	3139	3160	3181	3201	2	4	6	8	11
2.1	3222	3243	3263	3284	3304	3324	3345	3365	3385	3404	2	4	6	8	10
2.2	3424	3444	3464	3483	3502	3522	3541	3560	3579	3598	2	4	6	8	10
2.3	3617	3636	3655	3674	3692	3711	3729	3747	3766	3784	2	4	5	7	9
2.4	3802	3820	3838	3856	3874	3892	3909	3927	3945	3962	2	4	5	7	9
2.5	3979	3997	4014	4031	4048	4065	4082	4099	4116	4133	2	3	5	7	9
2.6	4150	4166	4183	4200	4216	4232	4249	4265	4281	4298	2	3	5	7	8
2.7	4314	4330	4346	4362	4378	4393	4409	4425	4440	4456	2	3	5	6	8
2.8	4472	4487	4502	4518	4533	4548	4564	4579	4594	4609	2	3	5	6	8
2.9	4624	4639	4654	4669	4683	4698	4713	4728	4742	4757	1	3	4	6	7
3.0	0.4771	4786	4800	4814	4829	4843	4857	4871	4886	4900	1	3	4	6	7
3.1	4914	4928	4942	4955	4969	4983	4997	5011	5024	5038	1	3	4	6	7
3.2	5051	5065	5079	5092	5105	5119	5132	5145	5159	5172	1	3	4	5	7
3.3	5185	5198	5211	5224	5237	5250	5263	5276	5289	5302	1	3	4	5	6
3.4	5315	5328	5340	5353	5366	5378	5391	5403	5416	5428	1	3	4	5	6
3.5	5441	5453	5465	5478	5490	5502	5514	5527	5539	5551	1	2	4	5	6
3.6	5563	5575	5587	5599	5611	5623	5635	5647	5658	5670	1	2	4	5	6
3.7	5682	5694	5705	5717	5729	5740	5752	5763	5775	5786	1	2	3	5	6
3.8	5798	5809	5821	5832	5843	5855	5866	5877	5888	5899	1	2	3	5	6
3.9	5911	5922	5933	5944	5955	5966	5977	5988	5999	6010	1	2	3	4	6
4.0	0.6021	6031	6042	6053	6064	6075	6085	6096	6107	6117	1	2	3	4	5
4.1	6128	6138	6149	6160	6170	6180	6191	6201	6212	6222	1	2	3	4	5
4.2	6232	6243	6253	6263	6274	6284	6294	6304	6314	6325	1	2	3	4	5
4.3	6335	6345	6355	6365	6375	6385	6395	6405	6415	6425	1	2	3	4	5
4.4	6435	6444	6454	6464	6474	6484	6493	6503	6513	6522	1	2	3	4	5
4.5	6532	6542	6551	6561	6571	6580	6590	6599	6609	6618	1	2	3	4	5
4.6	6628	6637	6646	6656	6665	6675	6684	6693	6702	6712	1	2	3	4	5
4.7	6721	6730	6739	6749	6758	6767	6776	6785	6794	6803	1	2	3	4	5
4.8	6812	6821	6830	6839	6848	6857	6866	6875	6884	6893	1	2	3	4	4
4.9	6902	6911	6920	6928	6937	6946	6955	6964	6972	6981	1	2	3	4	4
5.0	0.6990	6998	7007	7016	7024	7033	7042	7050	7059	7067	1	2	3	3	4
5.1	7076	7084	7093	7101	7110	7118	7126	7135	7143	7152	1	2	3	3	4
5.2	7160	7168	7177	7185	7193	7202	7210	7218	7226	7235	1	2	2	3	4
5.3	7243	7251	7259	7267	7275	7284	7292	7300	7308	7316	1	2	2	3	4
5.4	7324	7332	7340	7348	7356	7364	7372	7380	7388	7396	1	2	2	3	4
5.5	7404	7412	7419	7427	7435	7443	7451	7459	7466	7474	1	2	2	3	4
5.6	7482	7490	7497	7505	7513	7520	7528	7536	7543	7551	1	2	2	3	4
5.7	7559	7566	7574	7582	7589	7597	7604	7612	7619	7627	1	2	2	3	4
5.8	7634	7642	7649	7657	7664	7672	7679	7686	7694	7701	1	1	2	3	4
5.9	7709	7716	7723	7731	7738	7745	7752	7760	7767	7774	1	1	2	3	4

LOGARITHMS OF NUMBERS FROM 6.00 TO 9.99 AND BY INTERPOLATION FROM 6.000 TO 9.999

	0	1	2	3	4	5	6	7	8	9	Interpolation 1	2	3	4	5
6.0	0.7782	7789	7796	7803	7810	7818	7825	7832	7839	7846	1	1	2	3	4
6.1	7853	7860	7868	7875	7882	7889	7896	7903	7910	7917	1	1	2	3	4
6.2	7924	7931	7938	7945	7952	7959	7966	7973	7980	7987	1	1	2	3	3
6.3	7993	8000	8007	8014	8021	8028	8035	8041	8048	8055	1	1	2	3	3
6.4	8062	8069	8075	8082	8089	8096	8102	8109	8116	8122	1	1	2	3	3
6.5	8129	8136	8142	8149	8156	8162	8169	8176	8182	8189	1	1	2	3	3
6.6	8195	8202	8209	8215	8222	8228	8235	8241	8248	8254	1	1	2	3	3
6.7	8261	8267	8274	8280	8287	8293	8299	8306	8312	8319	1	1	2	3	3
6.8	8325	8331	8338	8344	8351	8357	8363	8370	8376	8382	1	1	2	3	3
6.9	8388	8395	8401	8407	8414	8420	8426	8432	8439	8445	1	1	2	3	3
7.0	0.8451	8457	8463	8470	8476	8482	8488	8494	8500	8506	1	1	2	2	3
7.1	8513	8519	8525	8531	8537	8543	8549	8555	8561	8567	1	1	2	2	3
7.2	8573	8579	8585	8591	8597	8603	8609	8615	8621	8627	1	1	2	2	3
7.3	8633	8639	8645	8651	8657	8663	8669	8675	8681	8686	1	1	2	2	3
7.4	8692	8698	8704	8710	8716	8722	8727	8733	8739	8745	1	1	2	2	3
7.5	8751	8756	8762	8768	8774	8779	8785	8791	8797	8802	1	1	2	2	3
7.6	8808	8814	8820	8825	8831	8837	8842	8848	8854	8859	1	1	2	2	3
7.7	8865	8871	8876	8882	8887	8893	8899	8904	8910	8915	1	1	2	2	3
7.8	8921	8927	8932	8938	8943	8949	8954	8960	8965	8971	1	1	2	2	3
7.9	8976	8982	8987	8993	8998	9004	9009	9015	9020	9025	1	1	2	2	3
8.0	0.9031	9036	9042	9047	9053	9058	9063	9069	9074	9079	1	1	2	2	3
8.1	9085	9090	9096	9101	9106	9112	9117	9122	9128	9133	1	1	2	2	3
8.2	9138	9143	9149	9154	9159	9165	9170	9175	9180	9186	1	1	2	2	3
8.3	9191	9196	9201	9206	9212	9217	9222	9227	9232	9238	1	1	2	2	3
8.4	9243	9248	9253	9258	9263	9269	9274	9279	9284	9289	1	1	2	2	3
8.5	9294	9299	9304	9309	9315	9320	9325	9330	9335	9340	1	1	2	2	3
8.6	9345	9350	9355	9360	9365	9370	9375	9380	9385	9390	1	1	2	2	3
8.7	9395	9400	9405	9410	9415	9420	9425	9430	9435	9440	0	1	1	2	2
8.8	9445	9450	9455	9460	9465	9469	9474	9479	9484	9489	0	1	1	2	2
8.9	9494	9499	9504	9509	9513	9518	9523	9528	9533	9538	0	1	1	2	2
9.0	0.9542	9547	9552	9557	9562	9566	9571	9576	9581	9586	0	1	1	2	2
9.1	9590	9595	9600	9605	9609	9614	9619	9624	9628	9633	0	1	1	2	2
9.2	9638	9643	9647	9652	9657	9661	9666	9671	9675	9680	0	1	1	2	2
9.3	9685	9689	9694	9699	9703	9708	9713	9717	9722	9727	0	1	1	2	2
9.4	9731	9736	9741	9745	9750	9754	9759	9763	9768	9773	0	1	1	2	2
9.5	9777	9782	9786	9791	9795	9800	9805	9809	9814	9818	0	1	1	2	2
9.6	9823	9827	9832	9836	9841	9845	9850	9854	9859	9863	0	1	1	2	2
9.7	9868	9872	9877	9881	9886	9890	9894	9899	9903	9908	0	1	1	2	2
9.8	9912	9917	9921	9926	9930	9934	9939	9943	9948	9952	0	1	1	2	2
9.9	9956	9961	9965	9969	9974	9978	9983	9987	9991	9996	0	1	1	2	2

INCHES TO CENTIMETERS, EQUIVALENTS

Inches	*Centimeters*	*Inches*	*Centimeters*
50	127.0	66	167.6
51	129.5	67	170.2
52	132.0	68	172.8
53	134.6	69	175.3
54	137.3	70	177.8
55	139.6	71	180.4
56	142.2	72	182.9
57	144.7	73	185.4
58	147.4	74	188.0
59	149.0	75	190.5
60	152.4	76	193.0
61	155.0	77	195.5
62	157.5	78	198.0
63	160.0	79	200.5
64	162.6	80	203.0
65	165.1		

SECONDS TO DECIMAL PARTS OF A MINUTE, EQUIVALENTS

Secs.	*Mins.*	*Secs.*	*Mins.*	*Secs.*	*Mins.*
1	.02	21	.35	41	.68
2	.03	22	.37	42	.70
3	.05	23	.38	43	.72
4	.07	24	.40	44	.73
5	.08	25	.42	45	.75
6	.10	26	.43	46	.77
7	.12	27	.45	47	.78
8	.13	28	.47	48	.80
9	.15	29	.48	49	.82
10	.17	30	.50	50	.83
11	.18	31	.52	51	.85
12	.20	32	.53	52	.87
13	.22	33	.55	53	.88
14	.23	34	.57	54	.90
15	.25	35	.58	55	.92
16	.27	36	.60	56	.93
17	.28	37	.62	57	.95
18	.30	38	.63	58	.97
19	.32	39	.65	59	.98
20	.33	40	.67	60	1.00

POUNDS TO KILOGRAMS, EQUIVALENTS

Lbs.	*Kgs.*	*Lbs.*	*Kgs.*	*Lbs.*	*Kgs.*	*Lbs.*	*Kgs.*
60	27.2	128	58.2	196	89.1	264	120.0
62	28.1	130	59.1	198	90.0	266	120.9
64	29.0	132	60.0	200	90.9	268	121.8
66	30.0	134	60.9	202	91.8	270	122.7
68	30.9	136	61.8	204	92.7	272	123.6
70	31.8	138	62.7	206	93.6	274	124.5
72	32.7	140	63.6	208	94.5	276	125.5
74	33.6	142	64.5	210	95.5	278	126.4
76	34.5	144	65.5	212	96.4	280	127.3
78	35.4	146	66.4	214	97.3	282	128.2
80	36.3	148	67.3	216	98.2	284	129.1
82	37.2	150	68.2	218	99.1	286	130.0
84	38.1	152	69.1	220	100.0	288	130.9
86	39.0	154	70.0	222	100.9	290	131.8
88	40.0	156	70.9	224	101.8	292	132.7
90	40.9	158	71.8	226	102.7	294	133.6
92	41.8	160	72.7	228	103.6	296	134.5
94	42.7	162	73.6	230	104.5	298	135.5
96	43.6	164	74.5	232	105.5	300	136.4
98	44.5	166	75.5	234	106.4	302	137.3
100	45.5	168	76.4	236	107.3	304	138.2
102	46.4	170	77.3	238	108.2	306	139.1
104	47.3	172	78.2	240	109.1	308	140.0
106	48.2	174	79.1	242	110.0	310	140.9
108	49.1	176	80.0	244	110.9	312	141.8
110	50.0	178	80.9	246	111.8	314	142.7
112	50.9	180	81.8	248	112.7	316	143.6
114	51.8	182	82.7	250	113.6	318	144.5
116	52.7	184	83.6	252	114.5	320	145.5
118	53.6	186	84.5	254	115.5	322	146.4
120	54.5	188	85.5	256	116.4	324	147.3
122	55.5	190	86.4	258	117.3	326	148.2
124	56.4	192	87.3	260	118.2	328	149.1
126	57.3	194	88.2	262	119.1	330	150.0

CENTIGRADE TO FAHRENHEIT, EQUIVALENTS

°*C.*	°*F.*	°*C.*	°*F.*	°*C.*	°*F.*	°*C.*	°*F.*
10	50	16	61	22	72	28	83
11	52	17	63	23	74	29	84
12	54	18	65	24	75	30	86
13	55	19	66	25	77	31	88
14	57	20	68	26	79	32	90
15	59	21	70	27	81	33	92

CALORIES TO OXYGEN PER MINUTE, EQUIVALENTS

Heat produced per hour, and per 24 hours, and the Equivalent Consumption of Oxygen per Minute for a Respiratory Quotient of 0.82 and a Calorific Value of Oxygen of 4.825 Calories per Liter.

Heat	*Produced*	*Oxygen*	*Heat*	*Produced*	*Oxygen*	*Heat*	*Produced*	*Oxygen*
Per	*Per 24*	*Per*	*Per*	*Per 24*	*Per*	*Per*	*Per 24*	*Per*
Hour	*Hours*	*Minute*	*Hour*	*Hours*	*Minute*	*Hour*	*Hours*	*Minute*
Cals.	*Cals.*	*C. C.*	*Cals.*	*Cals.*	*C. C.*	*Cals.*	*Cals.*	*C. C.*
31 .0	744	107	51 .0	1224	176	71 .0	1704	245
31 .5	756	109	51 .5	1236	178	71 .5	1716	247
32 .0	768	111	52 .0	1248	180	72 .0	1728	249
32 .5	780	112	52 .5	1260	181	72 .5	1740	250
33 .0	792	114	53 .0	1272	183	73 .0	1752	252
33 .5	804	116	53 .5	1284	185	73 .5	1764	254
34 .0	816	117	54 .0	1296	187	74 .0	1776	256
34 .5	828	119	54 .5	1308	188	74 .5	1788	257
35 .0	840	121	55 .0	1320	190	75 .0	1800	259
35 .5	852	123	55 .5	1332	192	75 .5	1812	261
36 .0	864	124	56 .0	1344	193	76 .0	1824	262
36 .5	876	126	56 .5	1356	195	76 .5	1836	264
37 .0	888	128	57 .0	1368	197	77 .0	1848	266
37 .5	900	130	57 .5	1380	199	77 .5	1860	267
38 .0	912	131	58 .0	1392	200	78 .0	1872	269
38 .5	924	133	58 .5	1404	202	78 .5	1884	271
39 .0	936	135	59 .0	1416	204	79 .0	1896	273
39 .5	948	136	59 .5	1428	206	79 .5	1908	274
40 .0	960	138	60 .0	1440	207	80 .0	1920	276
40 .5	972	140	60 .5	1452	209	80 .5	1932	278
41 .0	984	142	61 .0	1464	211	81 .0	1944	280
71 .5	996	143	61 .5	1476	212	81 .5	1956	282
42 .0	1008	145	62 .0	1488	214	82 .0	1968	283
42 .5	1020	149	62 .5	1500	216	82 .5	1980	285
43 .0	1032	149	63 .0	1512	218	83 .0	1992	286
43 .5	1044	150	63 .5	1524	219	83 .5	2004	288
44 .0	1056	152	64 .0	1536	221	84 .0	2016	290
44 .5	1058	154	64 .5	1548	223	84 .5	2028	292
45 .0	1080	155	65 .0	1560	225	85 .0	2040	294
45 .5	1092	157	65 .5	1572	226	85 .5	2052	295
46 .0	1104	159	66 .0	1584	228	86 .0	2064	297
46 .5	1116	161	66 .5	1596	230	86 .5	2076	299
47 .0	1128	162	67 .0	1608	232	87 .0	2088	301
47 .5	1140	164	67 .5	1620	233	87 .5	2100	302
48 .0	1152	166	68 .0	1632	235	88 .0	2112	304
48 .5	1164	167	68 .5	1644	237	88 .5	2124	306
49 .0	1176	169	69 .0	1656	238	89 .0	2136	308
49 .5	1188	171	69 .5	1668	240	89 .5	2148	309
50 .0	1200	173	70 .0	1680	242	90 .0	2160	311
50 .5	1212	174	70 .5	1692	244	90 .5	2172	313

The above table is computed from the formula $O = \frac{C \times 1000}{4.825 \times 1440}$ where C is the heat per 24 hours in calories, and O is the oxygen per min. in c.c.

CHAPTER 29

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CHAPTER 30

INDEX

This index includes references and cross references to chapter titles, paragraph headings, important subdivisions, authors, definitions, and tables.