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CONTENTS

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INVESTIGATIONS AT THE NUTRITION LABORATORY OF THE CARNEGIE INSTITUTION OF WASHINGTON, BOSTON, MASSACHUSETTS[1]

CONTRARY to popular opinion the researches of the Carnegie Nutrition Laboratory do not follow for the most part the conventional lines of "nutrition investigations" with special emphasis upon the economic and sociological phases of the work. The admirable facilities and equipment of the United States Department of Agriculture fortunately make this unnecessary. The Carnegie Laboratory is, however, an outcome of the national nutrition investigations, for the late Professor W. O. Atwater, who was a pioneer in nutrition investigations of this country, wisely devoted a part of the government appropriation for nutrition investigations to an abstract study of the physiological effects of various nutrients upon the human body. This work was carried out in the chemical laboratory of Wesleyan University, Middletown, Conn., and resulted in the construction of a special form of apparatus for studying both the respiratory products and the direct heat production of man, an apparatus properly designated by Professor Atwater as a "respiration calorimeter." Subsequently the board of trustees of the Carnegie Institution of Washington authorized the construction of a special laboratory for similar research in Boston.

It was believed that the appropriation for this laboratory, for a time at least, could best be subdivided into three main

[1] An address delivered before the department of chemistry at Vassar College, Poughkeepsie, New York, on May 10, 1915.

categories: First, the development of new apparatus and technique, thus insuring progress in technical lines; second, the accumulation of normal physiological data regarding the metabolism and many physiological factors of both men and animals, such research being needed to supplement the insufficient data secured in previous investigations; and third, the comprehensive, critical study of certain pathological cases, notably diabetics. In connection with the first of these lines of work there has been not only the development of a large amount of apparatus—for the greater part of the apparatus used in the nutrition laboratory has been there devised and constructed—but also an extensive comparison of other methods in regular use, to determine their degree of accuracy and applicability.

The laboratory building is of special construction, the main feature being the large room devoted to calorimetric researches. With so delicate an apparatus as the calorimeter, the effect of temperature environment is profound, and consequently this room is provided with heating and cooling devices by which the temperature may be held constant. Researches with this apparatus may therefore be conducted at any time of the year without regard to the prevailing temperature.

As at present equipped, the calorimeter laboratory has four calorimeters, all of which may be used for studying the heat production of the human body. Of these the bed calorimeter has been most extensively used for studying normal men and women as well as in a long series of experiments with severe diabetics. The inner chamber of this apparatus is copper-walled and about 7 feet long and 3 feet wide, varying in height from 2 feet at the foot to about $3\frac{1}{2}$ feet at the head. The subject, lying comfortably on a mattress, is slid into this chamber and the opening closed with a large piece of plate glass, the closure being made airtight by sealing with wax. The ventilating current draws the air from this chamber, forces it through sulphuric acid to remove the water vapor given off by the lungs and skin of the subject, and then through soda lime to remove the carbon dioxide. After pure oxygen has been added to replace that used, the air returns to the chamber to be rebreathed by the subject. By weighing the soda lime containers at the beginning and end of the experiment and metering the oxygen admitted, we have a direct measure of the carbon dioxide produced and the oxygen consumed. This is the respiratory feature of the apparatus.

The method of measuring the heat production is of particular interest. The inner chamber or copper box is surrounded by several layers of material which provide good insulation. Outside of this copper box are two supplementary walls, the first of zinc and the second of a one-inch layer of cork. These walls are in each case three inches from the inner wall, providing two dead air spaces between the copper and the zinc and the zinc and the cork, respectively. The outside of the calorimeter is finished with compo board. Thus, the apparatus is of the refrigerator type of construction, effectually preventing heat radiation. In winter, houses are heated by passing hot water through pipes. This small chamber, or little house, would, unless cooled, become uncomfortably warm from heat given off by the body, and provision for cooling is made by passing a current of cold water through the chamber in fine serpentine copper pipes. The temperature of the water is recorded as it enters and leaves the chamber. If the total weight of water leaving the apparatus is measured the heat brought away is readily computed by multiplying this weight by the temperature difference.

The chair calorimeter is of a different shape, although primarily of the same construction. In the chair calorimeter, the subject sits in a comfortable arm chair, the walls of the chamber being of such a form as to give a minimum amount of air space about the body. The total volume of air space in the bed calorimeter is 950 liters, and in the chair calorimeter 1,500 liters. Neither apparatus, however, permits long experiments.

A third calorimeter has been built which is long enough for a man to lie down in, and yet high enough for him to stand up; the form of the chamber also permits the installation of a bicycle ergometer inside the chamber for muscular work experiments. The volume of air space in this apparatus has been limited to 3,500 liters. By means of a double port-hole it is possible to put in or take out food or other material without loss of air. The subject can live in this apparatus as long, if not longer, than in the chamber at Wesleyan University, Middletown, Conn., the longest experiment with that apparatus covering 13 days and 14 nights. Thus far no continuous calorimeter experiments of any considerable length have been made in the Nutrition Laboratory.

Finally, to provide a calorimeter especially designed for severe muscular work with a bicycle ergometer, treadmill, or endless ladder, a calorimeter has been built with provision for installing any one of these muscular work appliances. Owing to the great amount of heat that will be developed in such experiments, special heat-absorbing pipes and temperature measuring apparatus have been necessary.

With the respiration calorimeter it is possible to measure simultaneously the carbon dioxide and water vapor produced, the oxygen consumed, and the heat given off by a man. These factors taken not only individually, but also together, give most important data for the computation of the character and amount of the interchange of material inside of the body due to vital processes.

Fortunately it was found that the long and costly twenty-four-hour calorimeter experiments could be in part replaced by shorter experiments, in which only the carbon-dioxide production and oxygen consumption were studied, by means of a respiration apparatus devoid of calorimetric features and that this type of short experiment could be used in the study of many problems. An apparatus was devised by which a subject lying on a bed could breathe through a mouth- or nosepiece, and determinations of the carbon dioxide produced and the oxygen consumed could be made in periods as short as 15 minutes. These experiments have been carried out very rapidly and at relatively slight expense, and have been of great value in giving us a large amount of important physiological information. In recent years, the calorimeters have also been used for short experiments, these being from one to two hours long; indeed, the research on diabetes, which has been in progress in the Nutrition Laboratory for the past six years, has relied for the most part on calorimeter experiments of from one and one half to two hours' duration.

The influence of muscular activity upon the production of carbon dioxide and heat is enormous. When a subject is sound asleep, quiet and without food in the stomach, we have the minimum basal metabolism. The influence of sleep has only been tardily recognized, and the majority of physiologists are inclined to speak of basal metabolism as that obtained in the early forenoon, when the subject is lying quietly without breakfast, but not asleep. If the subject is sitting up, the metabolism is increased, and if he is doing work it is increased in proportion to the amount of work. The approximate normal output of carbon dioxide and heat for a man of average weight with varying conditions of muscular activity is shown in Table I. By means of this table one may calculate the approximate carbon dioxide and heat output of a man during twenty-four hours. (See Table II.)

TABLE I

Average Normal Output of Carbon Dioxide and Heat from the Body

Conditions of Muscular Activity	Average Quantities Per Hour: Carbon Dioxide, Gm.	Heat Cals.
Man at rest, sleeping	25	65
Man at rest, awake, sitting up	35	100
Man at light muscular exercise	55	170
Man at moderately active muscular exercise	100	290
Man at severe muscular exercise	150	450
Man at very severe muscular exercise	210	600

TABLE II

Average Daily Output of Heat of a Man at Light Muscular Work

Daily Program	Heat Output
At rest, sleeping, 8 hours, 65 calories per hour	520
At rest, awake, sitting up, 6 hours, 100 cal. per hour	600
Light muscular exercise, 10 hours, 170 cal. per hour	1,700
Total output of heat, 24 hours	2,820

It is of no avail to make investigations in pathology unless we have a suitable base line or ground for comparison, and in practically all our clinical studies we have had to supply the deficiency in normal data. While the temptation is at times very great to carry out a series of experiments which will most certainly promise striking results, we have felt constrained to plod along and secure fundamental basal values, and thus contribute steadily to the knowledge of the physiology of man. To do this, and to secure information as to the influence of variations in height, age, weight and sex of normal individuals, we have studied 90 or more normal men, and nearly as many normal women, and have secured approximate basal values for these individuals. Studies have likewise been made of athletes and vegetarians. For the most part these observations were made with the small respiration apparatus and not with the calorimeters; indeed, at times as many as four respiration apparatus have been used simultaneously in our large calorimeter room, in studying the metabolism of four individuals.

Two factors that affect normal metabolism more than any others are the ingestion of food and muscular activity. In Table I., the somewhat vague terms of "light," "moderately active," "severe" and "very severe" muscular work were used. These really have no quantitative meaning, and it is necessary for us to measure accurately the amount of mechanical work performed when studying the metabolism of a person doing severe muscular work. For this purpose several forms of bicycle ergometer have been used by means of which the rider transforms a certain amount of muscular work into heat. The ergometer may be placed inside a respiration calorimeter, or the subject may be connected with a suitable mouthpiece to a simple respiration apparatus. The series of studies on this apparatus have proved most illuminating, and show that the human body is really a very efficient engine. While in certain cases as much as 35 per cent. of the total energy transformed during muscular work may be transferred to the pedals of the ergometer, there to be transformed into heat, the average values obtained were those given in Table III.

TABLE III

Experiments on Bicycle Riders (Calories per Hour)

	Resting	Working	Work Done	Efficiency, Per Cent.
J. C. W. (college athlete)	112	339	49	21.6
B. F. D. (college athlete)	106	318	45	21.2
A. L. L. (untrained)	—	326	46	20.8
E. F. S. (untrained)	?	399	51	18.1
N. B. (professional rider)	92	619	112	21.3
		471	79	20.8
		401	65	21.0
		382	60	20.7

The figures in Table III. shed a most interesting light on the question of training. It has commonly been supposed that when a person is trained, the muscles become more effective and consequently there is a greater production of work for the same expenditure. Here we find that in the first place the two men, A. L. L. and E. F. S., who were wholly untrained, and indeed wholly unfamiliar with the bicycle, accomplished as much work as did the college athletes, J. C. W. and B. F. D., with an efficiency very little less than that of the first two. When we examine the results obtained with the professional bicycle rider, Mr. Nat Butler, we find that he was able by virtue of his strength to accomplish a very great deal *more* work than any of the other men, but as a matter of fact his *efficiency* was not materially greater than that of the college athletes, or, indeed, the untrained men.

In order to produce this heat in the body there must have been vigorous combustion, either of body substance, in case the subject did not have food enough, or of food material previously eaten. We have found as a result of a large number of experiments that a man at rest, doing no visible external muscular work, requires not far from 2,000 calories for maintenance during twenty-four hours. It will be seen that in three hours Mr. Butler produced nearly this amount when at severe muscular work; consequently he must have burned up in these three hours as much material as would ordinarily be burned by a subject at rest in twenty-four hours. On this same basis, he would need three meals every three hours or one square meal an hour.

A new series of muscular work experiments is in progress in the Nutrition Laboratory under the direction of Professor H. M. Smith in which the subject walks on a specially-designed treadmill at varying rates of speed, breathing through a mouthpiece into a respiration apparatus which measures the carbon-dioxide excretion and the oxygen consumption. As a result of this investigation it has been found that in walking on a level road at a moderate gait (70 to 80 meters per minute) there is an increase in the heat production for each kilogram of body weight moved forward one meter, which is equivalent to about 0.5 small calorie. With an increase in velocity the energy expenditure is rapidly augmented and during running may become 60 per cent. more per unit of weight transported than that of the subject walking at a moderate rate. Studies are also being made with this treadmill in which the subject walks on an incline, the work of ascent thus being added to the work of walking on a level.

In this investigation, which is elaborate, a large number of simultaneous measurements have been attempted. In addition to measurements of the carbon-dioxide excretion and the oxygen consumption, we have simultaneously recorded the total distance walked, the number of steps, the inclination of the treadmill and the total height of the body movement. By attaching a cord to the shoulders and connecting it with a pointer, a record of the up-and-down motion of the body with each step is made, and by a multiplying device the total sum of the upward motions of the body are also recorded, thus giving the total height to which the body is raised during the period of walking, for in walking on a level plain, an individual raises his body from 1 to $1\frac{1}{2}$ inches each step.

Connected with the ventilating air current of the respiration apparatus is a delicately-counterpoised bell or gas-holder, which rises and falls with each respiration. By means of a pointer attached to the counterpoise of this bell, a graphic record of the type of respiration is obtained. A multiplying device attached permits the measurement of the total amount of air actually passing through the lungs independent of the ventilation of the respiration apparatus itself. This graphic record of the ventilation of the lungs likewise records the respiration rate. Finally, by means of electrodes attached to the chest, the pulse rate of a walking man is photographically recorded with a string galvanometer or an oscillograph.

The intimate relationship between pulse-rate and the total energy output has been the subject of special study, and the pulse-rate, the respiration-rate, and particularly the body temperature have received especial attention in our several lines of investigation. The distribution of a number of delicate thermometers in different parts and cavities of the body has shown that when the temperature deep in the body trunk undergoes its regular daily rhythm, these fluctuations in temperature are accompanied by similar fluctuations in all the other thermometers, and that while the absolute temperatures in different parts of the body are unlike, the fluctuations in temperature are essentially the same throughout the whole body.

It has long been known that when food is eaten the body activities are considerably increased. This is particularly the case when the food consists of protein material. The exact cause of this increase has long been the subject of much discussion. On the one hand it was believed that this was due to the work of digestion in the digestive tract; on the other hand, that it was due to an excess heat production caused by the splitting off and combustion of portions of the protein molecule. A long series of investigations in the Nutrition Laboratory has shown that when peristaltic stimuli, such as saline purgatives, were used and careful control tests made, the movements of the digestive tract did not measurably increase the metabolism. When dogs who had deficient digestive capacity were fed large amounts of meat, in spite of the excess of undigested residue, the metabolism was not augmented. Evidence has been accumulated which shows that the acid products of cleavage in the processes of digestion are probably the chief factors causing this increase in metabolism, which was explained by the direct stimulus of the cells to a greater activity.

One of the most interesting researches developing from the comparison of methods for studying the respiratory exchange has been the importance of knowing physiologically the exact composition of outdoor air. Every person is continually taking air into the lungs. Many technical methods for determining the amount of oxygen thus consumed involve some assumption as to the exact composition of the normal outdoor air inhaled. An investigation lasting over three years, in which daily analyses of outdoor air were made by Miss Alice Johnson, proved conclusively that the percentage of carbon dioxide and oxygen in uncontaminated outdoor air remained constant throughout the entire year, irrespective of wind direction and temperature. Specimens of normal air secured at numerous places on the Atlantic Ocean and on the top of Pike's Peak showed the same remarkable uniformity. By this study we were provided at one and the same time with a standard for testing all gas-analysis apparatus and definite knowledge regarding the composition of inspired air, thus doing away with the necessity for the innumerable analyses that otherwise would be essential.

The investigations on diabetes in conjunction with Professor Elliott P. Joslin have shown in the first place that during severe diabetes there is a distinct increase in the basal metabolism of the patients. It has also been shown that this increased metabolism in diabetes is due to the fact that with the abnormal breaking down of food materials in the body of the diabetic there is developed an excessive amount of acid, chiefly B-oxybutyric acid, which directly stimulates the cells to a greater activity. With treatment reducing the acidity and particularly with the new, remarkable Allen treatment this increased metabolism entirely disappears.

In addition to the study of diabetics, a number of other projects have received consideration at the Nutrition Laboratory. Among these are the study in conjunction with Dr. F. B. Talbot of the metabolism of normal and atrophic infants and of infants in the first hours of post-natal life. The importance of knowing the energy requirements and the character of the combustion in the body of the new-born infant has justified an extended research on this subject in which we have studied over 100 infants within the first few hours after birth. The new-born babies were taken from the hospital immediately after birth, placed in the respiration chamber and there studied for several hours, very careful records of the carbon dioxide produced and the oxygen consumed being made. The observations on atrophic hospital infants have supplied values of particular significance in interpreting a number of so-called "physiological laws." Indeed, one of the best methods of studying physiology is to study abnormal physiology.

In connection with the respiration experiments on infants a knowledge of the exact degree of repose of the subject is of importance. I have already shown the enormous influence of severe muscular activity upon the metabolism of man, and it is evident that if, in securing normal data regarding infants, to be subsequently used for comparison with pathological cases, we do not take cognizance of the influence of even minor muscular activity, we are liable to great error. Thus, it would be wholly irrational to compare the metabolism of a normal, healthy infant, but moving and restless, with that of a weak, emaciated infant lying perfectly quiet. Nor is it sufficient to supplement our measurements of the respiratory exchange by records of ocular observations of the activity, for experience quickly showed us that these were wholly inadequate. A method has therefore been devised for automatically recording the muscular activity. The crib in which the baby is placed rests at one end on two frictionless steel points. The other end is supported by a spiral spring having a rubber tube about it. As the infant moves, the air inside of the rubber tube expands or contracts and by means of the air transmission any changes in this tension may be recorded with a delicate tambour and writing point. This adjustment may be so delicate that even the slight change in the center of gravity of the infant due to respiration, muscular tremors, or movements of the hand or fingers are immediately recorded. These graphic records are now an absolute essential of all metabolism experiments in our laboratory, and unless the records of activity are approximately alike, no use is made of the experimental periods for comparison purposes. Precisely this same principle applies not only to babies, but to the observations on animals, such as dogs, ducks, geese and guinea pigs. Arrangements are made for securing similar records for men and women lying in the bed calorimeter or on a couch connected with the respiration apparatus.

A large number of observations have been made on normal animals, chiefly dogs, rabbits, and more recently geese. The influence of partial inanition, of temperature environment, of the ingestion of various kinds of foods, and of living in an atmosphere containing a high percentage of oxygen have all been the subject of researches which are more or less nearly complete. It was obviously necessary to develop special apparatus and special technique for these researches and in all instances the observations included a large number of control tests of the apparatus and experiments with control animals.

While many, if not indeed the majority of the researches in the Nutrition Laboratory may be considered as of an abstract, scientific nature, one research certainly has far-reaching, practical bearings, namely, the investigation of the influence of alcohol upon the metabolic, neural and muscular processes. The laboratory is at present engaged in an extended program of research on these vexed problems and not only is the influence of alcohol upon the metabolic processes studied with the special equipment of the laboratory, but a special laboratory has been constructed for the study of the influence upon the neural and muscular processes. The equipment of this special laboratory includes the exceedingly ingenious string galvanometer of Einthoven for measurements of the pulse and heart, the faradic stimulus apparatus of Kronecker and of Martin, and particularly the apparatus of Dodge. In the past year the psychological phases of the work have been further extended by Professor Walter R. Miles to include observations on professional typists, with a most careful analysis of the movements and reactions incidental to typewriting. A program for the complete research has been prepared and submitted to a large number of European and American scientists for comment, and the studies will be planned in accordance with this program. Such an elaborate program emphasizes the value of being able to conduct researches continuously for a series of years and thus accumulate definite and authoritative data with regard to problems that have heretofore been studied for the most part in a desultory manner.

Perhaps the most ambitious undertaking of the laboratory thus far has been a recent study of prolonged fasting. Just prior to the establishment of the Carnegie Nutrition Laboratory a special fund was appropriated by the trustees of the Carnegie Institution of Washington for the study of fasting at Wesleyan University, Middletown, Conn. Upon the basis of this investigation plans were made for studying a fasting subject over a long period, but it was not until 1912 that opportunity arose for satisfactorily conducting such a research. The subject fasted for a period of thirty-one days, taking absolutely no food and drinking but 900 c.c. of distilled water per day. The subject was also studied during a short preliminary period and during a three-day realimentation period. During

[NUTRITION LABORATORY OF THE CARNEGIE INSTITUTION OF WASHINGTON, BOSTON, MASSACHUSETTS]

METABOLISM CHART OF A MAN FASTING 31 DAYS

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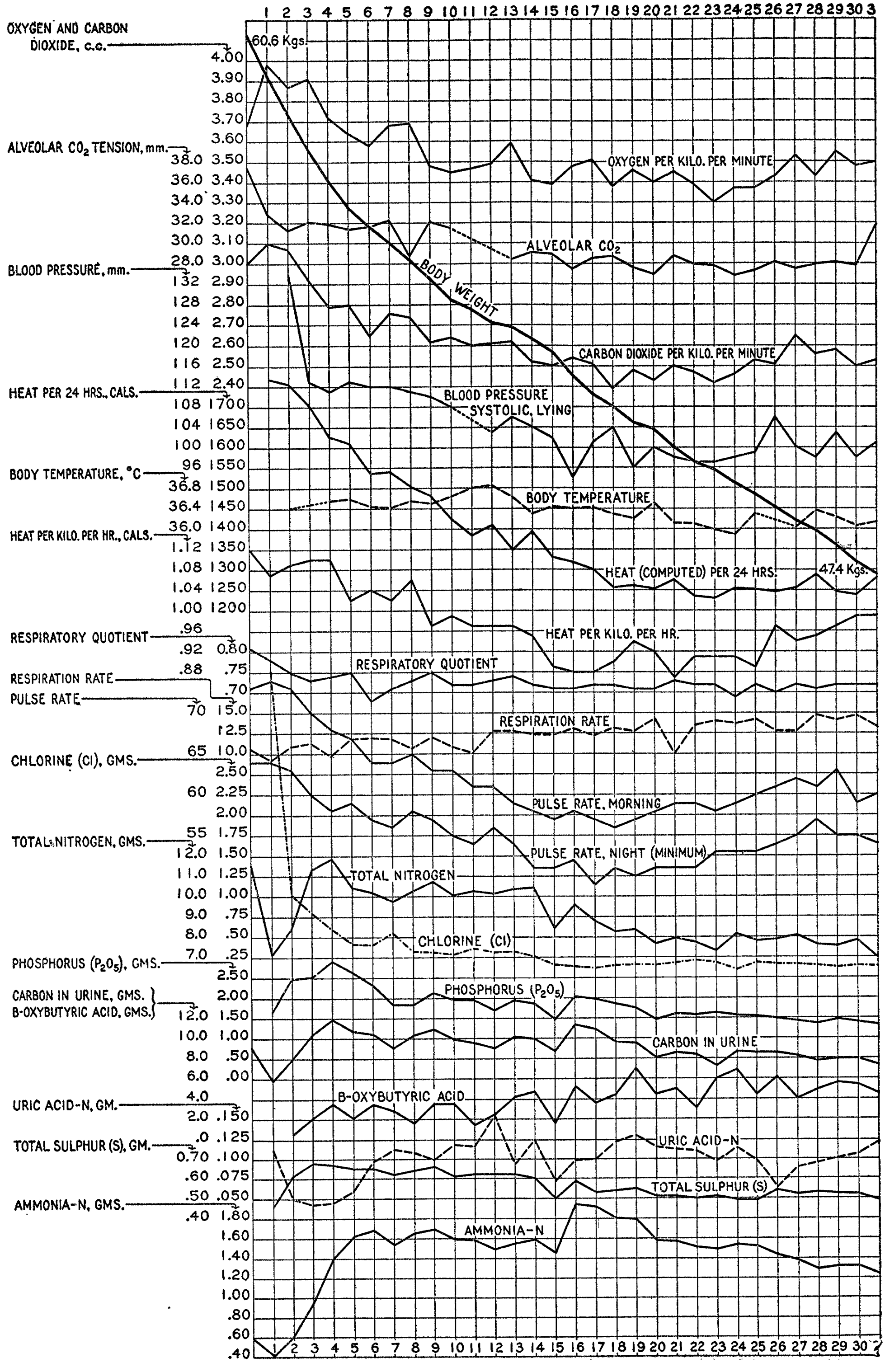

the sojourn of the subject in the laboratory, the entire laboratory staff, with a corps of medical experts, was concentrated upon securing simultaneous observations with this subject. A large number of observations of a purely physiological nature were made, such as body-weight, insensible perspiration, temperature fluctuations, pulse-rate, blood pressure and certain observations on the mechanics of respiration. The gaseous metabolism and the alveolar air were also measured. The subject slept each night throughout the experiment for approximately 10 hours inside of the bed calorimeter. He was under surveillance constantly and it was therefore impossible for him to secure any food. As a result he lived entirely upon body substance, and chemical analyses, which included a study of the gaseous, solid and liquid excreta, gave most important data regarding the breaking down of the material inside the body, and the various components most strenuously attacked as a result of the fasting.

The subject was an ideal one, remaining very quiet. Comparisons of the metabolism and other factors during sleep and during waking were thus perfectly feasible for the first time, and showed the profound influence of sleep upon the metabolism. From the numerous experiments with both the respiration apparatus and the respiration calorimeter and a careful record of the daily activity, the total balance of income and outgo of this man for thirty-one days could be computed with great accuracy. The most important factors of metabolism measured on this subject are indicated on the accompanying chart.

Simultaneous with the physiological and chemical examination, an important psychological study showed that for thirty-one days the subject was able to exist in a fairly normal mental condition. A most rigid and careful clinical examination was made every other day and the subject was under the constant supervision of skilled physicians. All the resources of the laboratory were brought to bear upon this study and the whole project illustrates in the best manner possible the particular advantages of a laboratory of this type and the peculiar obligations of workers in the laboratory to undertake in so far as possible only those researches that can not be satisfactorily studied elsewhere.

Francis G. Benedict

NEANDERTAL MAN IN SPAIN: THE LOWER JAW OF BAÑOLAS

It is not generally realized that the first skeletal remains of what is now known as *Homo neandertalensis,* or Mousterian man, were found in Spain at Gibraltar in 1848. This preceded the discovery in the valley of the Neander by nine years. In many respects the Gibraltar skull is still one of the most important specimens of this type of early man. Although its distinctive characters were early recognized by both Falconer and Busk, the discovery of the man of Neandertal coming at a more opportune time was the first to win and hold the attention of the scientific world: hence for the name of that race we have *Homo neandertalensis* instead of *H. calpicus* (from Calfé, the old name for Gibraltar).

The history of the Gibraltar skull is almost paralleled by that of another discovery in Spain, not near Gibraltar but in the northeasternmost province, Gerona, near the eastern end of the Pyrenean chain of mountains. Some 23 km. north-northwest of Gerona, the capitol of the province of the same name, in the center of a depression lies the lake of Bañolas, now only a remnant of what it once was. Immediately to the east of the southern end of the lake is the town of Bañolas built on travertine beds left by the former greater lake. These rest on early Quaternary red clays and have been exploited extensively for building purposes. The quarry of Don Lorenzo Roura is near the northern limits of the