From the groups of men and women it was possible to make selections of a number of individuals who had approximately the same height and weight; on this basis alone can an intelligent comparison be made. Eleven groups, with body weights varying from 67 kg. to 45 kg., were compared and it was found that the average heat-production of all eleven groups, computed on the basis of per kilogram of body weight, was 26.5 calories with men and 25.0 calories with women. The heat output of the men was greater in all but three of the eleven groups.

Using again the computation on the basis of the heat production per square meter of body surface we found that the average for the eleven groups showed 819 calories per 24 hours for the men as compared with 770 calories for the women. Of the eleven groups only two had lower values for the men than for the women.

On the basis of the foregoing paper, giving the results of a study of athletes, we rigorously excluded athletes from these comparisons, and hence we are dealing here with non-athletic men and women of the same height and the same weight. It is thus reasonable to suppose that the actual body surface of the different groups must have been very nearly the same, and it is not logical to assume that the larger heat production noted with the men was due to a disproportion between the body measurements and the body surface. We believe that these data show a basal metabolism for men some 5 or 6% greater than for women of similar height and weight, and that this increase is due to the fact that in all probability the women, particularly in those groups with the greater body weight, had a much larger proportion of subcutaneous fat than did the men, thus indicating a consequent smaller proportion of active protoplasmic tissue.

The detailed report of this investigation has been transmitted to the *Journal of Biological Chemistry.*

THE FACTORS AFFECTING NORMAL BASAL METABOLISM

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Although it is well known that the basal normal metabolism of individuals varies considerably, the exact cause for these variations is not known. For many years physiologists have believed that the heat production of a living body is proportional to the surface area. This most helpful hypothesis served to bring order out of chaos in the earlier

study of energy requirements and transformations in the living organism, but as experimental evidence accumulated, the validity of this so-called 'law of surface area' has been frequently called into question. An extended series of observations on 89 men and 68 women, all of them normal individuals in presumably good health, together with observations upon a group of athletes, a large number of new-born infants, normal infants under one year, and atrophic infants, and particularly a recent 31-day study of a fasting man, have given us data which warrant a reconsideration of the factors affecting basal metabolism.

When all of the observations on the normal men and women are plotted on charts, it is seen that there is no direct relationship between body weight and the total metabolism other than that, in general, people of large body weight have a greater metabolism than smaller individuals. However, there are so large a number of exceptions to this general rule that nothing approximating a physiological law can be derived from these observations. The same is true with regard to the computations of the heat production per kilogram of body weight, for the widest variations are found with our so-called normal people, with no tendency towards uniformity. Furthermore, it has been shown in a foregoing article that the total metabolism and the metabolism per kilogram of body weight are distinctly larger with athletes than with normal individuals. In all of these comparisons the differences between men and women have been recognized; hence separate plots for men and women have been made.

It has been practically impossible to make direct surface measurements of the men and women that we have studied, and we have relied, as have all physiologists hitherto, upon the commonly accepted formula of Meeh, in which the body surface is considered to be the cube root of the square of the weight multiplied by the constant 12.312. For infants the slightly smaller constant of 10.3, determined by Lissauer, has been accepted as the best available. Using Meeh's formula, we find that the metabolism of normal men, as computed from the body surface and expressed in calories per square meter of body surface per 24 hours, ranged from 693 to 958 calories. Since, according to the currently accepted belief in the constancy of heat production per square meter of body surface, we would expect to find constant values with all individuals, irrespective of size, it can be seen that this variation is extraordinarily large. It should furthermore be stated that both of these extremes were found with non-athletic individuals. With women the range was from 633 calories per square meter per 24 hours to 906 calories.

In neither of these comparisons is there any tendency to regularity or to a grouping of the plots. In other words, the evidence all points towards distinct individuality with no relationship between the computed body surface and the heat production.

With infants the variations in the metabolism on this basis are even greater. Thus it was found with normal and atrophic infants that the 24-hour heat production per square meter ranged from 554 calories to 1334 calories, while with the strictly normal infants the range was from 554 to 991 calories. It is obvious that any basis of comparisons which involves possible variations of 40% with men, 43% with women and 80% with normal infants cannot be considered as a physiological law.

On the other hand, an examination of the available material shows that there is a relationship between the heat production and the body composition, that is, that any physiological data which imply a difference in the proportion of active protoplasmic tissue are invariably accompanied by a difference in the basal metabolism. Thus the trained athletes showed a distinctly greater metabolism than did the non-athletic individuals. Furthermore, men with a smaller amount of subcutaneous fat and a correspondingly greater proportion of active protoplasmic tissue have been found to have a greater metabolism than women of the same height and weight. The study of normal and atrophic infants showed that with two infants of the same height and weight the elder, who would naturally be somewhat atrophic, invariably had a higher basal metabolism than the normal, well-nourished infant. Even with normal adults it can be maintained that of two individuals having the same weight but different heights, the taller individual will, in general, have the greater proportion of active protoplasmic tissue and the comparison of the heat production of normal men of like age and weight but different heights shows that there is almost invariably a distinctly greater metabolism with the taller individual. It should be remembered that in all of these comparisons only the basal metabolism, measured in complete muscular repose and in the post absorptive condition, is used.

A factor that has heretofore been neglected in considering basal metabolism is the possibility that the mass of active protoplasmic tissue may functionate with varying degrees of intensity. In comparing the metabolism of normal individuals we find that frequently individuals with approximately the same weight had very great variations in the heat production. This is true of a group of eight men weighing over 80 kgm. and likewise with a group of five men weighing 50 kgm. or under.

This, of itself, points strongly towards distinct differences in the intensity of cellular activity.

While the larger proportion of individuals studied were in youth, i.e., 20 to 30 years of age, a few were under 17 and a number over 40. On studying the plots showing the variations with normal individuals, both for men and women, a distinct tendency may be noted for the older people of both sexes to have a somewhat decreased metabolism. The evidence is equally as clear that in youth the metabolism is considerably increased, thus pointing towards an increased cellular activity in early youth and a decreased cellular activity or possible atrophy of active protoplasmic tissue with increasing age.

One of the most noticeable factors influencing metabolism is that of sleep. It has been commonly assumed that sleep *per se* does not affect metabolism, but it has been found in a long study of a fasting man that there were numerous metabolic planes during the day, showing that the stimulus to cellular activity must have varied considerably. With this fasting man neither the mass of protoplasmic tissue nor the surface area of the body could have altered materially in the course of 24 hours, yet we find that if we give a value of 100 to the basal metabolism during the night, when the subject was sound asleep, the value when the subject was lying awake in the morning, with complete muscular repose, would be 114, and in the late afternoon under the same conditions the value would be 122.

Our laboratory data include experiments with a considerable number of normal men covering several months, and in some cases, several years. A study of these data shows that the metabolism of 35 subjects on whom experiments were made 5 days or more apart and, on the average, several months apart, varied not far from 14%, although in all cases the subject was in complete muscular repose and in the post absorptive condition. Since during this period there was no material alteration in the body weight and consequently in the body surface, the variation in the metabolism must be ascribed to a difference in the stimulus to cellular activity.

In the fasting experiment not only was there a difference in the metabolic level noted at different times of the day due to the condition of being awake and asleep, and in the late afternoon after the experimental program of the day, but, as the 31-day fast progressed, the heat production per square meter of body surface varied from 859 calories on the first fasting day to 668 calories on the twenty-third fasting day. Although the loss in body weight was material, apparently the skin shrank

in proportion and there was no obvious disproportion between body weight and surface area. During the fourth week of the fast there was a distinct tendency for the metabolism to rise, accompanied by a measurable increase in the pulse rate. Thus the tendency for the prolonged fasting to depress the metabolism was actually overcome by some unknown stimulus increasing the cellular activity of the remaining body substance, ultimately resulting in a positive increase in the basal metabolism during the last week of fasting.

Two other factors have been experimentally demonstrated in this laboratory as influencing the metabolism. One of these is the character of the preceding diet, it having been shown that when a carbohydrate-free diet is eaten an acidosis is developed which distinctly increases the cellular activity and results in a very noticeable increase in the basal metabolism. The second factor is the marked after-effect of severe muscular work, such work causing the pulse rate and the basal metabolism to remain at an increased level for many hours after the cessation of the muscular activity. This may logically be ascribed to a stimulus to the protoplasmic tissue, resulting in a higher metabolic plane.

From the evidence cited, therefore, it may be concluded that there is no direct relationship between total body weight and total heat production, that the metabolism or heat output of the human body, even at rest, does not depend upon Newton's law of cooling, and is therefore independent of the surface area. The observations on athletes, the comparison of normal men and women, and of atrophic and normal infants indicate that the proportion of active protoplasmic tissue plays an important rôle. Perhaps the most striking factors causing variations in the stimulus to cellular activity are age, sleep, prolonged fasting, character of the diet, and the after-effect of severe muscular work.

From the evidence gathered with the various subjects studied it is clear that the basal metabolism of an individual is a function, first, of the total mass of active protoplasmic tissue, and, second, of the stimulus to cellular activity existing at the time the measurement of the metabolism was made.

The detailed report of this investigation has been transmitted to the *Journal of Biological Chemistry*.