Acta Paediatrica Academiae Scientiarum Hungaricae Vol. 7 (2), pp. 105—128 (1966)

Determination of the Thermoneutral Environment of Marasmic Infants

By

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(Received September 1, 1965)

The dynamics of metabolism within each particular species is influenced by several specific factors [2], such as body surface, stature, posture and the environment. These specific factors are not the same in the erect man as in quadrupeds or birds [1]. Differences of this kind make it difficult to compare the energy metabolism of different species.

The energy metabolism of living organisms is influenced by environmental temperature. Organisms with developed regulatory mechanism, exposed to unusually low or high temperatures, are capable of adjusting their energy metabolism within certain limits. There exists a zone of temperature in which the metabolism of the resting organism remains at a relatively low level. This is the basal metabolism, and the zone of temperature is called neutral, indifferent or comfort zone [7]. The thermoneutral zone of all homothermic organisms is between 27° and 31°C [3, 52]. Changes of environmental temperature within these limits do not entail fluctuations in the intensity of metabolism demonstrable by the usual methods. The resting organism has no sensation of either heat or cold in the neutral zone which is around 29°C for the unclothed adult [3, 10, 45, 56] and — according to recent investigations — between 32° and 34°C for newborn, and between 34° and 36°C for premature, babies [4, 5, 6, 43, 44].

The present investigations had the purpose to ascertain the thermoneutral zone in respect to atrophic infants [18, 19, 27, 53]. The first step was to determine how the metabolism of underdeveloped infants, accustomed to a permanently higher temperature, would react to being transferred to an environment of 20° to 22°C, a milieu which represents the thermoneutral zone for adequately clothed eutrophic infants. It was further intended to observe how atrophic babies protect themselves from being cooled down at that — for them unusual — low temperature, one which under physiological conditions ought to increase metabolism. Another series of investigations had the object to study the acute effect of high environmental temperature on the thermogenesis of atrophic infants, to provide additional support to the earlier observation that, in contrast to eutrophic babies, marasmic infants kept in an adequately humid milieu of 28° to 30°C, increase their metabolism instead of reducing it [16, 26, 28]. This observation, together with the results of investigations concerning heat production in a permanently overheated environment, might be interesting from the angle of energy metabolism and thermoregulation.

Material and Method

The material of the study consisted of eutrophic, hypotrophic, moderately atrophic and gravely marasmic infants. Oxygen consumption, rectal temperature, the effect of low and high environmental temperature on oxygen consumption were observed; the study extended further to energy metabolism related to both actual and ideal weight. The energy metabolism of differently built marasmic infants was, moreover, compared with that of normal babies. Metabolic investigations were performed in air-conditioned boxes by means of a Noyons type diapherometer. Methods and technical details have been described earlier [15, 16, 28].

Part of the presented diagrams has been published earlier but a thorough analysis of the thermoneutral zone and a detailed discussion of pathologic thermoregulation have made its repeated presentation necessary.

Results

Fig. 1 shows data regarding heat production of 75 hypotrophic and atrophic infants according to age groups. The solid line indicates heat production in eutrophic, the circles that in atrophic infants. It is clear that the latter produce less heat than normal babies.

The shaded part of Fig. 2/a represents heat production in cal/kg of normal infants, the circles that of atrophic babies with weight-deficiencies between 20 and 40 per cent. Mean heat produced by such infants at room temperature was 57 cal.

Fig. 2/b shows mean heat production by the infants represented in Fig. 2/a, with reference to the normal body weight of eutrophic infants of the same length (called "eutrophic weight" in the following); it amounted to 42.3 cal/kg. A comparison of Figs 2/a and 2/b makes it clear that the latter presents a truer picture of reality than the former.

Data in Fig. 3/a are referred to the own body weight of the atrophic infants, while Fig. 3/b shows the same data with reference to eutrophic weight. The diagrams present heat production of 13 hypotrophic and 7 atrophic infants who had been accustomed to an adequately humid milieu of 29° to 30°C. It also shows heat production of the same babies after 60 and 150 minute exposures to temperatures between 16° and 22°C.

Data obtained at high and low temperatures are connected by solid lines in Figs 3/a and 3/b. When kept in a milieu of 29° to 30°C, no infant in any group had other clothing than a diaper. Diagram I of these figures shows data of infants with a weight deficiency of 13 to 20 per cent who were wrapped in swaddling clothes at a temperature of 17°C; the corresponding parameters for Diagram II

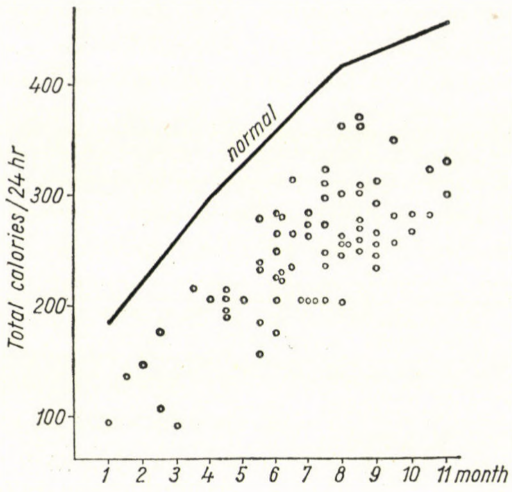

FIG. 1. Daily heat production of variously built infants according to age

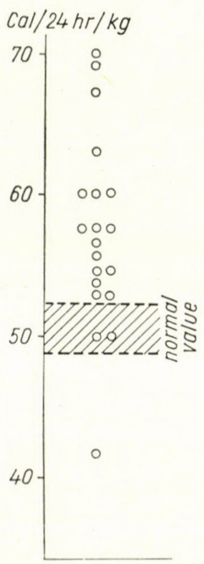

FIG. 2a. Heat production by infants with 20 to 40 per cent weight deficiency

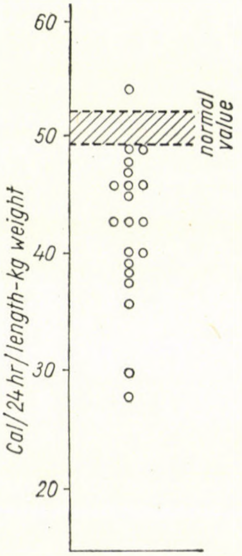

FIG. 2b. Heat production by atrophic infants represented in Fig. 2a, computed for heat production by eutrophic infants of the same length

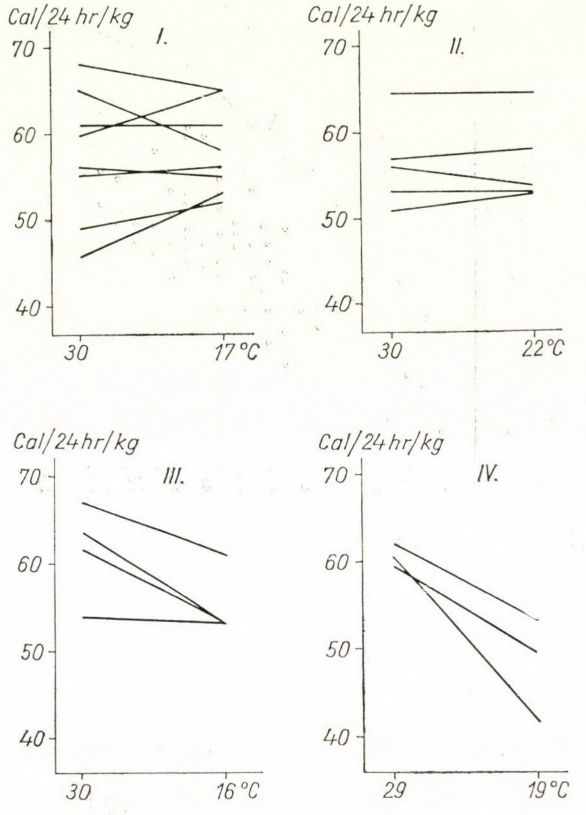

FIG. 3a. Heat production in cal/kg by differently clothed hypotrophic (I, II) and atrophic (III, IV) infants, adapted to adequately humid environment of 29° to 30°C, after a stay of 60 min. (I—III) and 150 min. (IV) in climatic units of 17° and 22°C or 16° and 19°C

are: 14 to 19 per cent weight deficiency, 22°C, clothed with a shirt and covered with a thin blanket; diagram III: 26 to 30 per cent weight deficiency, 16°C, swaddling clothes; diagram IV: 22 to 30 per cent weight deficiency, 19°C, shirt and diaper. Diagrams I and II represent babies who, by having been kept in a hot milieu and carefully nursed for 6 to 8 weeks, were gaining weight and had developed from atrophic to hypotrophic infants, whereas the severely atrophied babies represented in diagrams III and IV were still at the beginning of the upward path. The average value of heat production in adequately clothed infants of groups I and II underwent no statistically significant change after 60 min. in a milieu of usual or a somewhat lower temperature. The average fall of body temperature during the 60 min. amounted to 0.5°C. Clad in warm protective clothing, the babies of Groups III and IV lost 0.4°C body temperature during control tests that lasted one to two hours; the loss was 2.2°C if the

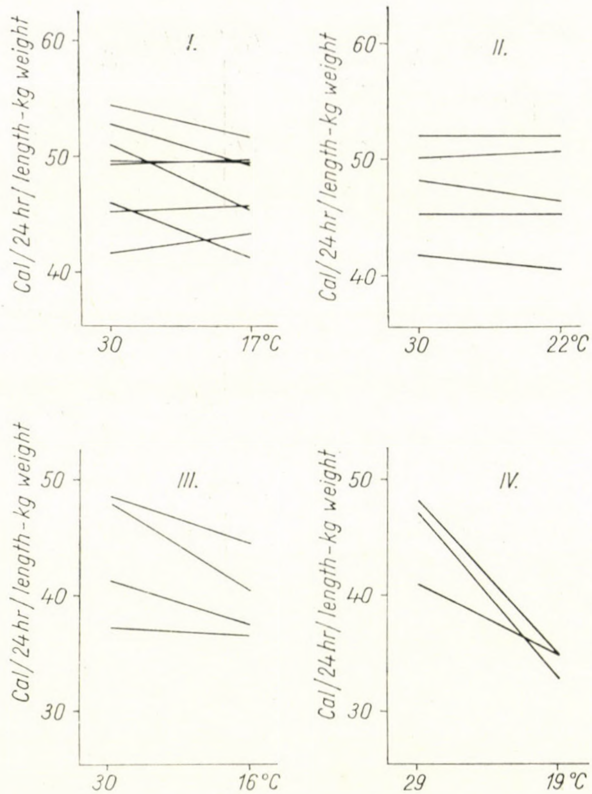

FIG. 3b. Heat production by the infants represented in Fig. 3a, computed for the weight of eutrophic infants of corresponding length

infants had no protective clothing although the temperature was relatively higher. The fall of body temperature was accompanied by a diminished heat production in both groups.

Fig. 4/a presents heat production of 22 atrophic and 14 hypotrophic infants kept in a milieu of 21 to 22°C, and also after a 24 hour stay in a comfortably humid milieu of 28 to 30°C. Values in Fig. 4/a are referred to actual, in Fig. 4/b to eutrophic body weight. Solid lines indicate the tendency and intensity of energy metabolism. Atrophic infants wore the usual clinical garments in the boxes of usual temperature, but had nothing on except a diaper in the high temperature climatic units. Group I consisted of babies with weight deficiencies between 26 and 40 per cent, Group II of babies with deficiencies of 20 to 25 per cent. A 24-hour stay in humid hot climate raised the energy metabolism by 13.1 per cent in the first, and by 12.0 per cent in the second group. The difference was significant statistically at a 0.1 per cent level of confidence. The change of climate did not affect average heat produc-

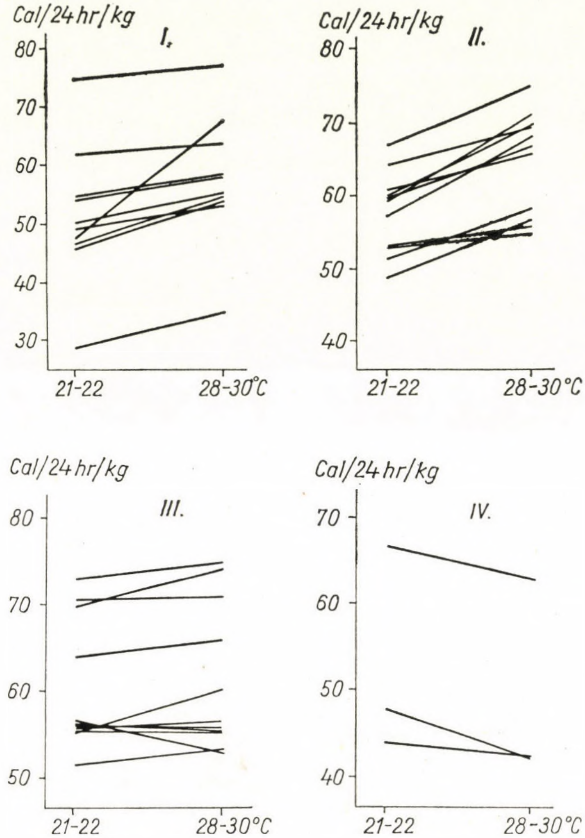

FIG. 4a. Heat production in cal/kg by atrophic (I, II), hypotrophic (III) infants, and infants with less than 5 per cent weight deficiency (IV), after 24 hrs stay in an environment of 28° to 30°C following prolonged stay in adequately humid atmosphere of 21° to 22° C. The infants had the usual clinical clothing at room temperature and were unclothed in the warm unit

tion in Group III composed of babies with weight deficiencies of 9 to 19 per cent ($p > 10$ per cent). Members of Group IV, composed of infants with weight deficiencies below 10 per cent, reacted to heat in the opposite sense; their energy metabolism, instead of increasing, showed an average decrease of 7.0 per cent.

Fig. 5/a presents heat production per kg body weight of 9 hypotrophic and moderately atrophic infants with weight deficiencies between 12 and 24 per cent (white column) and that of 11 gravely atrophic infants with deficiencies between 30 and 40 per cent (black column). Fig. 5/b shows the same data with reference to the ideal weight of an eutrophic infant corresponding to the body length of an atrophic infant. The first pair of columns shows the effect on heat production of a milieu of 20° to 22°C; the second pair indicates the immediate effect of an adequately humid climate of 28° to 30°C; the third pair of columns shows the effect of the same phied babies. It is nevertheless clear that heat production increased in both atrophic categories.

Fig. 6/a presents heat production per kg of actual body weight in dif-

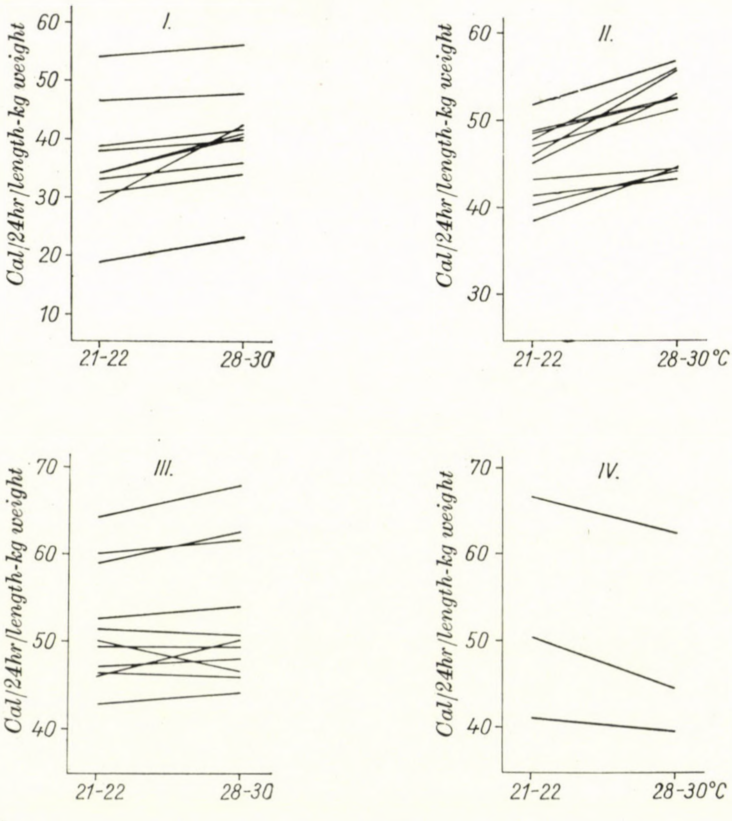

FIG. 4b. Heat production by infants represented in Fig. 4a, computed for weight of eutrophic infants of corresponding length

climate after 24, the fourth after 48, hours. Average heat production of infants with more than 30 per cent weight deficiency began at a deep point and increased by 25 per cent in 48 hours; despite this considerable rise, their heat production remained inferior to that of the averagely atro- ferently atrophied 20 babies (with weight deficiencies between 20 and 40 per cent, average 27.4 per cent) who had been kept for several months in an adequately humid atmosphere of 28° to 30°C. The shaded part of the diagram indicates the normal zone, the circles and dots show values

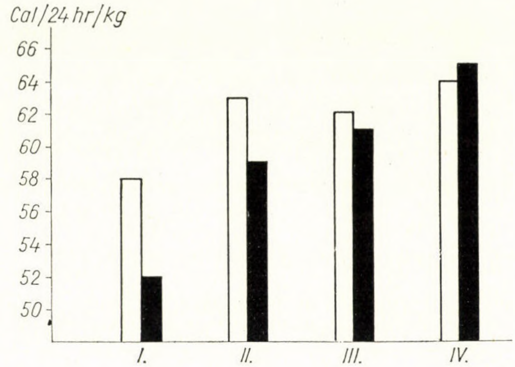

FIG. 5a. White columns indicate values for infants with weight deficiencies between 12 and 24 per cent; black columns show values for infants with weight deficiencies between 30 to 40 per cent. Columns No. I indicate heat production at 20° to 22°C; columns No. II indicate heat production immediately after transfer to an adequately humid atmosphere of 28° to 30°C; columns No. III show heat production after 24, columns No IV. after 48 hrs, in the warm milieu

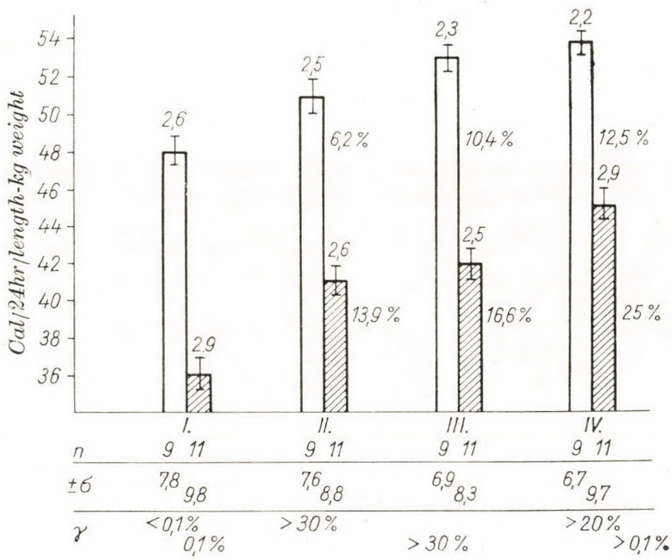

FIG. 5b. Heat production by the infants represented in FIG. 5a, as computed for body weight of eutrophic infants of corresponding length

for the same individuals in the hot climatic unit at the times indicated on the abscissa. Mean heat production by the marasmic infants was 57 cal/kg at the outset, 60 cal/kg after 18, and 63 cal/kg after 35 days.

Fig. 6/b presents the data of Fig. 6/a with reference to the ideal weight corresponding to the length of the atrophic infant. It can be seen that heat production at the maximum of atrophy was much below the average for

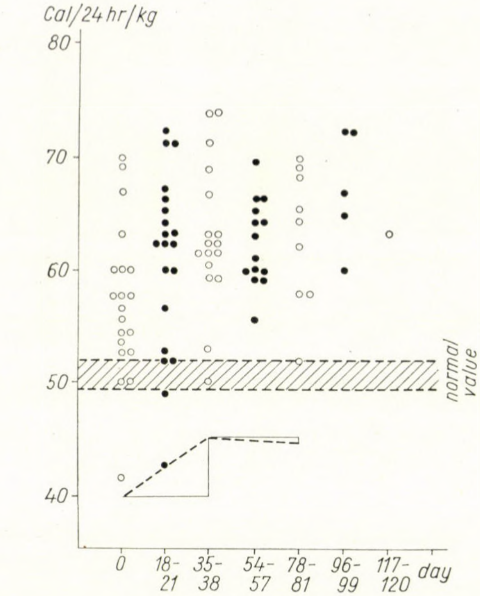

FIG. 6a. Heat production by infants with weight deficiencies between 20 and 40 per cent at various times (as plotted on the abscissa) during several months' stay in climatic units of 28° to 30°C

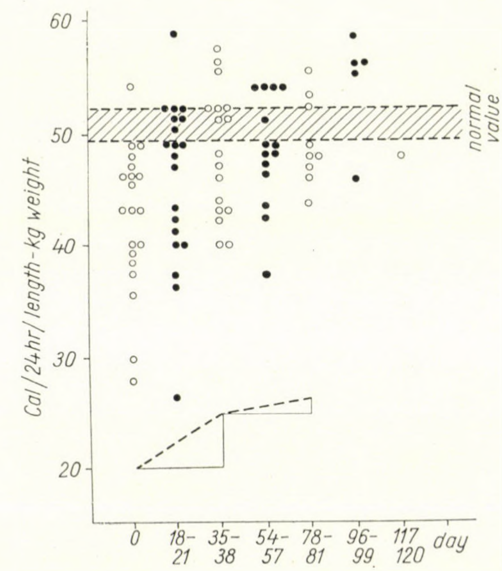

FIG. 6b. Values represented in Fig. 6a, as computed for kg body weight of eutrophic infants of corresponding length

eutrophic babies, and that — with advancing growth — the heat production of atrophic infants came gradually nearer to that of normal babies. The curve indicating the mathematical analysis of the values is in the lower part of the Figure. It is noteworthy that average heat production, as observed in the acute experiments and represented in Figs 4/b and 5/b, continued during the 5 weeks of the chronic experiments represented in Fig. 6/b, and — with advancing growth — had stabilized at a moderately high plateau considerably above the initial value. The value of heat produced by the atrophic infants rose, with reference to eutrophic weight, from the initial 42.3 cal to 45.7 on the 18th and to 48.2 on the 35th day of their stay in the climatic ward. The value on the 35th day approximated the physiological heat production of normal infants. The body weight of the atrophic babies rose from the initial average of 3765 g to 4003 and then to 4430 g on the 18th and 35th day, respectively.

Loss of weight during prolonged stay in a humid milieu of 28° to 30°C is presented in Fig. 7. The circles and dots indicate the times of measurements. Weight-loss at the points of time indicated on the abscissa in Figs 6/a and 6/b amounted to 27.4, 25.3, 23.0, 22.1, 20.9 per cent. The uniform downward gradient of the weight-loss curve means a correspondingly uniform progress of growth. It is evident from a comparison of Figs 6 and 7 that increase in the heat production of atrophic infants considerably surpassed the rate of growth in the first phase of their prolonged stay in a warm milieu.

Discussion

Views regarding the pathologic thermoregulation in infantile atrophy

The effect of a warm environment on basal metabolism is a subject that has been neglected even in respect of adult individuals [28, 52]. Except the present authors [15, 16] nobody seems to have studied the thermogenic effect on marasmic infants of a 24 to 48 hour or prolonged stay in a warm environment. It is only natural that, because of the novelty of the results, they have repeatedly met with scepticism and even downright refusal.

It was in 1952 that one of the present authors (L. K.) expounded the theory that, in cases of intact atrophy, the principal cause of growth failure was the pathological thermoregulation of atrophic infants [18, 19]. It took a whole decade of experiments to establish the fact that infantile atrophy is associated with pathologic thermoregulation, and to ascertain the thermoneutral zone of marasmic infants.

In 1955, at a conference on the problem of infantile marasmus, Kerpel-Fronius questioned the correctness of our theory which he seems to have misunderstood [13]. He wrote on another occasion (in 1960) that it was exaggerated on our part to regard the question of thermoregulation as the only problem of marasmus. He emphasized that the problem of thermoregulation was just one of the many complex aspects, admitting, however, that pathologic thermoregulation that it should be exactly the atrophic infant to behave in this manner [25]. Apart from the evidence of our experiments, this assumption is disproved by the fact that atrophic infants kept

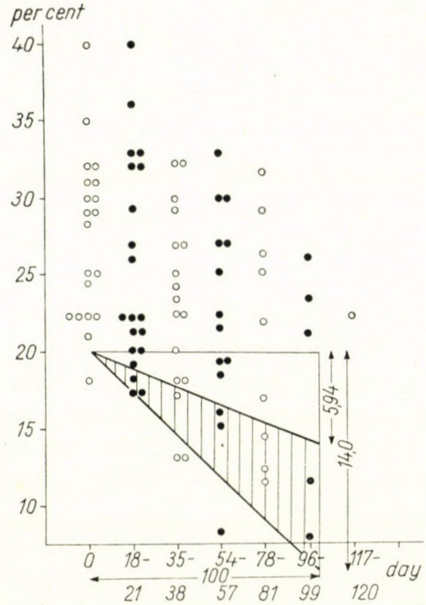

FIG. 7. Loss of weight of the marasmic infants represented in Figs 6a and 6b

may, in itself, restrict the possibility of repair. VÉGHELYI at the same time raised the question whether it was possible to determine the temperature to be considered neutral for marasmic infants and asked whether it was credible that conditioning for a single day should have so radically raised the metabolism of marasmic infants; he said that one is rather inclined to think the temperature of the conditioned milieu was above the indifferent zone and that the sudden rise of oxygen consumption was due to excessive heat; it being difficult to believe in a hot humid atmosphere do not display the usual signs of warming up such as restlessness, perspiration, hyperpnoea, flushing. Besides, quite a number of investigations have shown that in such milieu biological parameters tend to rise towards normal values [27].

The conclusion, based on acute experiments of a few hours' duration, that the thermoneutral zone of atrophic infants clad in the usual clinical garments lies between 22° and 28°C [54] is untenable, first, because a neutral temperature zone of such a wide range is unknown in human physiology and especially out of question with reference to infantile atrophy and, second, because — as seen from our diagrams — the calorie production by atrophic infants clad in clinical garments in a milieu of 22°C is subnormal and does not come even near to the amount of heat produced by them without clothing in a hot milieu.

Evaluation of the results

Total calorie production in the cases shown in Fig. 1 was invariably less than the heat produced by eutrophic infants of the corresponding ages. The growth index of babies in this group varied between 20 and 36, and their average body weight was 46 per cent less than that of the corresponding eutrophic infants. It has been generally recognized that total energy metabolism in the marasmic infant is inferior to that of normal babies of the same age [28], a natural phenomenon considering that marasmic infants have mostly half the body weight of their eutrophic counterparts.

The apparent contradiction between Figs 2/a and 2/b is due to a difference in the method of computation. Heat production, referred to the weight of atrophic infants (Fig. 2/a), extends beyond the normal zone, while heat production referred to that weight which would normally correspond to the given body length (Fig. 2/b), remains below normal. It was shown earlier [28] that the second method is preferable, and this the more so as only values obtained in this manner allow reliable comparisons between marasmic and eutrophic infants [51].

Body composition of atrophic infants differs from that of normal babies. Organs with high oxygen consumption (brain, kidney) are hardly affected by atrophy, while adipose tissues — organs of low energy consumption — practically disappear; muscle mass, the basis of chemical thermoregulation, is reduced; the volume of intracellular water is inferior, that of extracellular water superior, to the degree of atrophy. Anomalous phenomena of this kind have different degrees in the different atrophic subjects. Apart from the intensity of weight loss, the duration of the process of atrophy constitutes an important factor in this respect. Notwithstanding such discrepancies we had to adopt the method of referring heat production to the weight of eutrophic infants corresponding to the length of the given marasmic ones [30]. We have recognized in the course of serial investigations that the life functions of atrophic infants remain subnormal at the temperature customary in hospitals [27]. Complex investigations have definitely shown that in atrophic infants thermogenesis is essentially low [28, 29], a phenomenon evident from Fig. 2/b. Since it is clear that data regarding heat production and energy metabolism in atrophic infants express real conditions more truly if referred to the ideal weight corresponding to the height of the atrophic infant, we have based our following

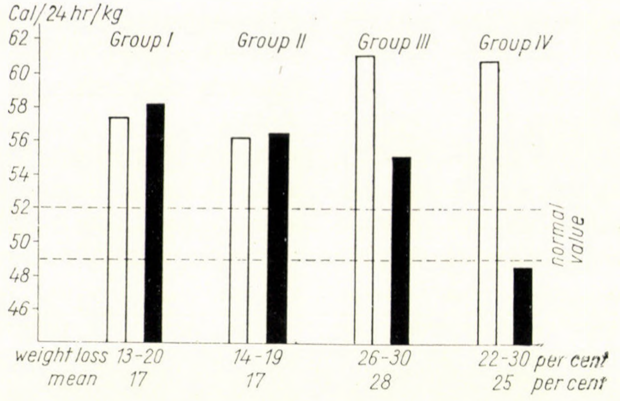

FIG. 8a. Average heat production computed from data in Figs. 3a and 3b, by unclothed atrophic babies in a permanently warm milieu of 29° to 30°C (white columns), and in climatic units of 16° to 22°C (black columns), with and without light clinical clothing, after a stay of 60 and 150 minutes

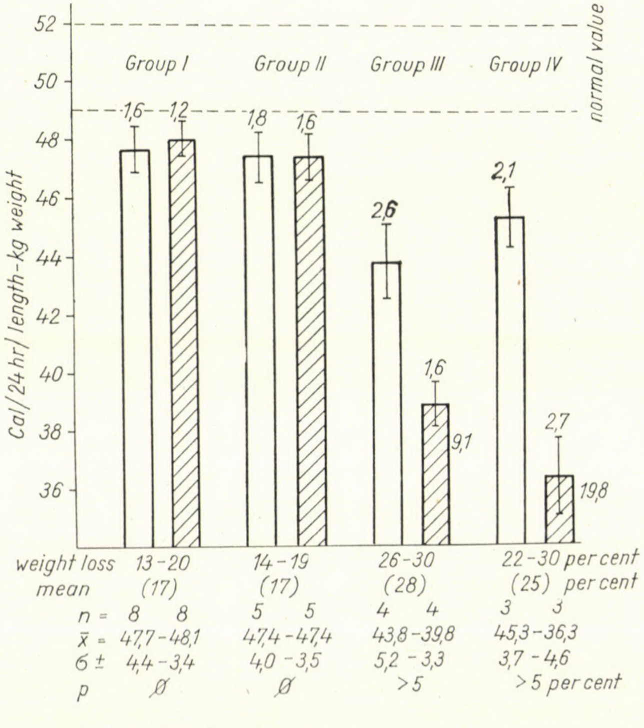

FIG. 8b. Data represented in Fig. 8a, as computed for kg body weight of eutrophic infants of corresponding length

analyses on data yielded by this method of computation.

Average experimental values

It is attempted in the following diagrams to approach the problem of thermoregulation in infantile atrophy by the analysis of mean values.

Figs 8/a and 8/b present the average values of Figs 3/a and 3/b. White columns indicate calorie production by atrophic infants in permanently warm climate, black and shaded columns show heat production during 60 minutes by differently atrophied and differently clothed babies at temperatures varying between 16 and 22°C. Values for Groups I and II prove that unclothed hypotrophic infants with weight deficiencies not exceeding 20 per cent, accustomed to high temperature, if kept for 60 min. at 17°C and provided with warm or lighter protective clothing, maintained the balance of energy metabolism while their body temperature decreased by 0.5°C. Group III was composed of babies with weight deficiencies exceeding 26 per cent; kept at 16°C for 60 min. and provided with warm protective clothing, both their heat production and body temperature showed a marked diminution. Members of Group IV were kept for 2 1/2 hours at 19°C without protective clothing; the average drop of body temperature was 2.2°C, while heat production decreased by 19.8 per cent. It is evident that atrophic infants, if kept at normal room temperature or lower temperatures, do not even try to increase heat production in order to maintain their body temperature, no matter how they are clothed.

Figs 9/a and 9/b present mean values for basal metabolism in 80 hypotrophic and atrophic infants at room temperature and in a warm milieu. The diagrams indicate heat production of marasmic infants (I) at room temperature; (II) measured immediately after transfer to an environment of 28°C to 30°; (III) measured after a stay of 24, and (IV) 48 hrs in the warm climate. If heat production is compared with weight-loss in Fig. 9/b, it is evident that — at room temperature (column I), in a certain phase of weight loss (Group III) — heat production lagged behind the corresponding eutrophic value, and that — with the progress of weight loss (Groups III—VII) — heat production continued to decrease. Heat production at room temperature in Groups VI and VII, i.e. in infants with the gravest marasmus, was considerably below normal. The growth index of Group I varied between 46 and 103. As regards heat production, members of this group (with an average weight deficiency of 5 per cent) behaved like normal babies. After a 24-hour stay in warm climate (column III), they reduced their energy metabolism to the lowest physiological limit. Heat production in Group II (average weight deficiency, 15 per cent) in the warm climate was not significantly different from the normal values measured at room temperature. Members of Groups III—VII—under the acute (II), 24-hour (III) and 48-hour (IV) effect of warm milieu —

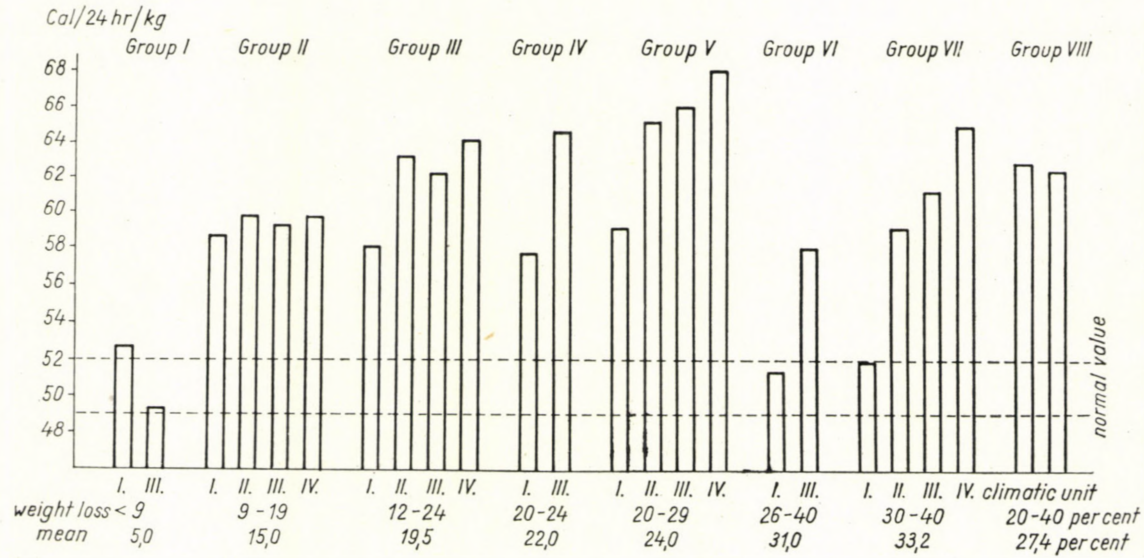

FIG. 9a. Combined effect of the degree of weight loss, environment of 20° to 22°C, and adequately humid milieu of 28° to 31°C, on heat production in marasmic infants. Columns No. I indicate values at room temperature, columns No. II those registered immediately after transfer to the warm milieu; columns No. III show values after a stay of 24, columns No. IV after one of 48 hours, in the conditioned units. Columns of Group VIII indicate average heat production by babies in the 5th and 8th week of conditioning; these infants had an average weight deficiency of 27.4 per cent before transfer to the climatic unit

raised their heat production practically in parallel with the progress of weight loss. Columns in respect of Group VIII show average heat production per kg in the 5th and 8th week of stay in warm milieu by babies whose weight deficiency amounted to 27.4 per cent prior to air conditioning. It can be seen that prolonged stay in a climate which for them was thermoneutral raised heat production of atrophic infants to approximately the lowest eutrophic level.

Optimum duration of the experiment

It has been found that the duration of acute experiments should not be restricted to one or two hours. As can be seen from Fig. 4/b (24-hour measurements), the percentual rise of heat production was almost identical in Group I (grave marasmus) and Group II (average atrophy): the difference was significant at a 0.1 per cent level of confidence. Energy metabolism showed increases of 13.0 and 10.5 per cent, respectively. Again, it is clear from Fig. 5/b that gravely atrophied babies, after a 48-hour stay in the warm milieu, raised their heat production by not less than 25 per cent. Prolonged acute experiments made it clear that even infants with weight deficiencies exceeding 30 per cent stepped up heat production dramatically, a phenomenon borne out by a comparison of Groups VI and VII in Fig. 9/b. All this shows that observations of a few hours' duration are not always reliable and should be evaluated with caution. On the other hand, it is not advisable to keep atrophic infants at a relatively low temperature for more than 3 hours, on account of possible noxious after-effects.

Thermoneutral zone of healthy adults, eutrophic and atrophic infants

It is generally recognized that the thermoneutral zone for unclothed adult humans is about 29°C [10, 45, 56]. Best and Taylor [3] designated the range 27—32.5°C as the thermoneutral zone.

This temperature is the same as that revealed by our experiments in respect of marasmic infants. The energy metabolism of the adult human remains unchanged, whereas that of unclothed atrophic babies is increased in this temperature zone. Customary clothing provides a thermoneutral environment for adults at room temperature, whereas atrophic infants are unable to maintain the physiological equilibrium of thermoregulation at room temperature, irrespective of their clothing.

Adequate protective clothing reduces surface loss of heat but does not prevent the loss via the respiratory system. The quotient body surface per volume amounts to 0.26 cm^{-1} for adults, 0.70 cm^{-1} for eutrophic newborns and 0.90 cm^{-1} for premature babies weighing 1500 g. The respiratory surface of adults measures 50 to 90 sq.m, but may even amount to 300 sq.m [8, 9, 17, 55] at a body surface of 1.73 sq.m. The ratio of respiratory surface and body surface of infants

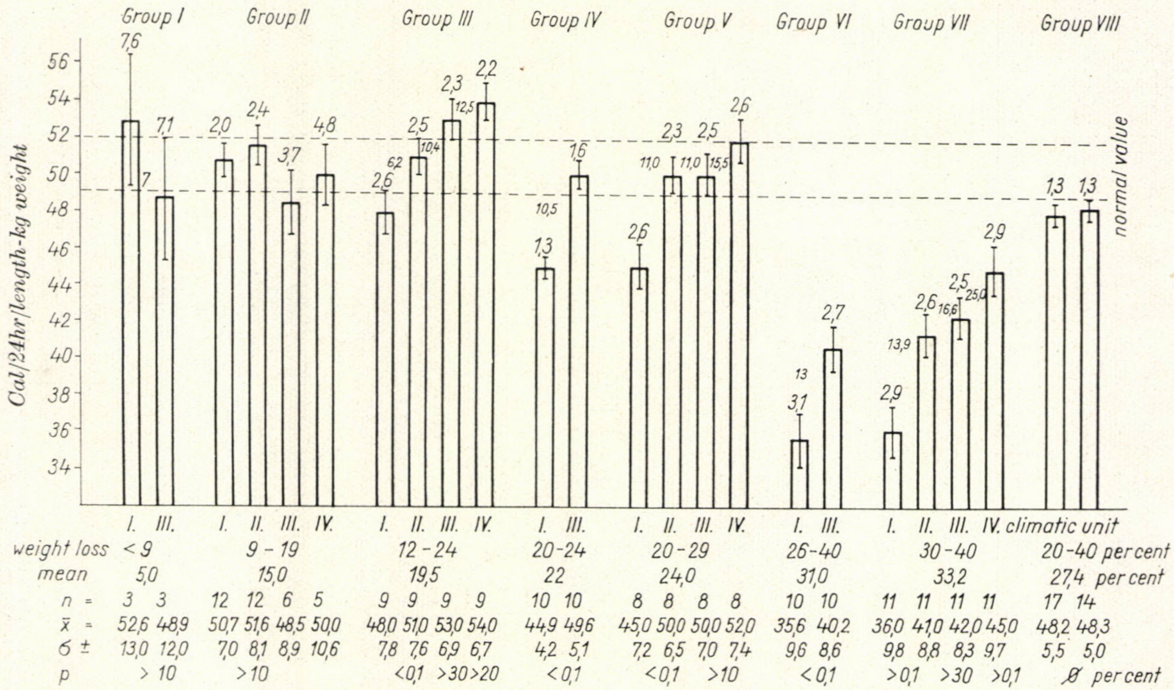

FIG. 9b. Data presented in Fig. 9a, as computed for kg body weight of eutrophic infants of corresponding length

is 13.4 sq.m/0.260 sq.m at the age of one month, 18.5/0.320 at 5 months and 52.5 sq.m/0.4 sq.m at 12 months [8]. Up to 6 months, the surface of the respiratory tract is 60 times, at 12 months 130 times, as large as body surface. Considering the significance of heat loss in the pathology of infantile marasmus, it makes a great difference whether the respiratory system, in continuous contact with the ambient atmosphere, inhales cool and dry or warm and adequately humid air.

Effect of ambient temperature on metabolic rate

It appears from Fig. 8/b (Groups III—VI) and Fig. 9/b (columns I), that, while staying in inadequately conditioned milieu, atrophic infants do not even try to reach that minimum of metabolic rate which is necessary for the maintenance of normal functions. As is evident from Fig. 8/b, atrophic babies, if exposed to lower ambient temperature, diminish the rate of energy metabolism instead of increasing it like normal infants. As can be seen (Fig. 9/b, columns I), infants with weight deficiencies exceeding 20 per cent are incapable of maintaining normal thermoregulation even at room temperature.

It is likewise clear from Fig. 9/b that the rate of energy metabolism decreased along with the growing disparity between body surface and body substance in a milieu of 20° to 22°C whereas — after a stay of 48 hours in an adequately humid atmosphere of 28° to 31°C — heat production in the same infants increased in proportion to the progress of atrophy. This observation justifies the conclusion that it is on account of the pathologic somatic condition that at an inadequate temperature energy metabolism follows Rubner's law in a paradoxical manner. Atrophic infants do not possess that reserve energy which is necessary for the maintenance of physiological thermoregulation in a cool milieu. It seems that — when atrophic infants suffer a pathologic loss of weight at normal room temperature — the heat impulses arriving from the body surface and the respiratory tract, i.e. the areas in contact with the ambient atmosphere, are inadequate during a well definable phase of the loss of body mass [30]; these impulses produce, via the hypothalamus, an inhibitory effect on the apparatus which maintains the physiological equilibrium of energy metabolism.

Effect of the environment on basal metabolism; analysis of the complex activities connected with metabolism

A survey of the functions closely connected with basal metabolism, examined under different climatic conditions in normal and pathological individuals, such as pituitary, thyroid and adrenal activity [32, 46, 50], circulation [14], carbohydrate [48], fat [33], and protein metabolism, nitrogen balance [23, 24], total alpha amino nitrogen [40], excretion of uric acid

[36], the behaviour of blood proteins and circulating proteins [37], plasma protein fractions [38], plasma volume, extracellular fluid compartment [35, 41], serum lipids [42], relative serum viscosity [39], and climatic factors [49], makes it obvious that the subnormal energy metabolism of marasmic babies under inadequate climatic conditions is an unavoidable consequence of the decrease in the supply of necessary food and body substances.

Subnormal energy consumption and the consequent reduction of functions *(vita minima)* mean a prolonged survival for the marasmic infants who, lacking the necessary amount of food and body substances, are staying in an inadequate milieu of room temperature. Pathologic thermoregulation is, essentially, a defence mechanism, a necessary phenomenon of adaptation [26].

Atrophic infants are chronically starving at room temperature [20]. They are — for both exogenous and endogenous reasons — unable to assimilate that amount of food which is necessary for the maintenance of normal body temperature and normal growth. They do not utilize the energy derivable from food in the same way as do normally growing babies. The atrophic organism converts a greater proportion of ingested food to heat than does the eutrophic one. It has been proved that, placed in an adequately humid atmosphere of 28 to 31°C, marasmic infants restore their reduced functions and start growing in a normal manner. It has been shown previously [27] that, in a warm climate, subnormal energy metabolism and thyroid activity become normal, circulation is accelerated, circulating blood volume is increased, oxygen supply, foodstuff transport, absorption and utilization are improved, appetite returns, and alimentary tolerance becomes wider. In an adequately humid warm milieu the pathologic thermoregulation of atrophic infants improves, and they are no longer compelled to convert to heat an abnormally large quota of the ingested food in order to maintain the required body temperature, and will be able to use for development the until then wasted excess. Data [19, 21, 24] according to which many atrophic infants failed to grow for weeks and months at room temperature in spite of receiving 110 to 130 calories/day/kg body weight, and started to develop normally when transferred to a climatic unit of 28° to 30°C, although there was no change in their diet, make it evident that the utilization of ingested food was different in the two environments. Eutrophic babies utilize of 110 calories about 25 for growth, and it seems that atrophic infants convert this amount of calories into heat if kept at room temperature, but utilize it like normal babies if kept in a warm milieu.

Earlier concepts

It was in 1952 that we made the following statement [19] on the sole evidence of bedside observations: "The pathologic condition of marasmic infants causes chemical and physical disturbances of the thermal equilibrium and gives rise to pathologic energy metabolism. 'Pathological thermoregulation' is the phenomenon which — after the elimination of all primary and interpolating causes — is solely responsible for atrophy and the lack of growth." "The organism does not build up owing to excessive rate of catabolism . . . disparity between the surface and the weight of the body compels the atrophic infant to employ excess chemical energy for the maintenance of body temperature." "Increased nutrition does not satisfy the high energy requirement of marasmic babies. The problem can be solved only if energy metabolism is normalized by a restoration of physiological thermoregulation. Chemical energy, liberated in this way, is incorporated by the organism of the marasmic infant who will accordingly start growing." Quotation from another earlier publication of one of the present authors [27]: "Unless an attempt is made to find our path in the labyrinth of numberless contradictory statements and results accumulated during many decades, we shall never be able to distinguish between functions which aggravate the basic pathologic process and those which ensure survival. The earlier statement [25] that a low metabolic rate is a favourable solution for the starving atrophic infant in his actual situation and in view of his future prospects of survival, was made in the conviction that adaptive dissimilative metabolism is bound to curtail life sooner or later unless a remedy is found to alleviate the inevitably developing grave situation".

Thermoneutral environment of the atrophic infant

The zone of environmental temperature in which energy metabolism remains unchanged at the lowest possible level is known as indifferent temperature. Fig. 9/b shows that this fundamental principle is true only up to a certain limit of weight deficiency [30], it being no longer valid if atrophy exceeds a certain point. Results, as illustrated in Figs 8/b and 9/b, justify the attempt to define the thermoneutral zone of marasmic infants. This zone lies in that temperature range where energy metabolism increases in proportion with the degree of atrophy and, stabilizing at a higher level, approaches the lowest eutrophic value. An adequately humid ambient atmosphere of 28° to 31°C seems to constitute the thermoneutral zone of infants with weight deficiencies over 19 per cent. It is, according to our observations, at this temperature that the minimal (i.e. physiological) rate of metabolism is stabilized [27].

In no other field of paediatrics (including the pathophysiology of prematures) does normal versus elevated temperature so deeply and in a so contradictory manner influence basal metabolism, and in no other branch has the study of the thermoneutral zone higher practical significance than in infantile atrophy.

Summary

Serial investigations made in marasmic infants of different body builds and in different stages of atrophy, have shown that once the disease responsible for the development and maintenance of marasmus has been cured, i.e. in intact atrophy, the central problem that remains and has to be overcome is a dysfunction of thermoregulation. A long chain of studies regarding the thermoneutral zone of marasmic infants has led to the conclusion that normal room temperature is inadequate for them, and that they are faced with an unsolvable task of producing and replacing heat if kept at such temperature.

The indifferent zone has been found to lie around 29°C for unclothed adults and marasmic infants alike. In an environment of such temperature, in adults the rate of metabolism remains stable at the lowest physiological level, whereas atrophic infants increase their metabolic rate. At room temperature, the usual clothing creates a thermoneutral environment for normal adults, whereas atrophic infants are not able to maintain the minimal physiological metabolic rate. Though wrapped in warm protective clothing, marasmic babies kept at room temperature do not even try to approach the minimal level of basal metabolism necessary for normal functions. Heat production by infants with an average weight deficiency of 33.2 per cent is about 30 per cent below the physiological level.

The thermoneutral zone for infants with weight deficiencies exceeding 19 per cent is a comfortably humid atmosphere of 28° to 31°C. Heat production in gravely atrophied babies transferred to such milieu showed a rise of 20 to 25 per cent in 48 hours.

Indifferent temperature is, according to the law of thermoregulation, that zone of the ambient temperature in which the metabolic rate remains unchanged at the minimal physiological level. It has, however, been found that the indifferent temperature for marasmic infants is that zone in which the hitherto subnormal metabolic rate suddenly begins to rise. The more advanced the atrophy, the more rapid the rise of metabolic rate. During the very first weeks of their stay in the conditioned climate, marasmic infants begin to grow and approximate the lowest eutrophic value of energy metabolism. Atrophic infants do not, therefore, follow the fundamental law of physiological thermoregulation.

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