

Survey of the essence of malnutrition on the basis of our thermoregulation research work

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The parameters of the vital functions prove beyond all doubt that, at the customary ward temperature, the vital functions of the true malnourished infants are subnormal; in contrast, in response to the thermoneutral climate at 29 °C, they accelerate and then normalize.

The disturbance of the thermal regulation, which develops in response to the extreme physical disparity of the malnourished infant and to the inadequate environment, is eliminated in the warm, comfort climate.

It was proved that the vital functions (neuroendocrinological function, basal metabolism, blood circulation, metabolism, absorption, utilization, assimilation, tolerance, etc.) approximate the physiological levels in this milieu. The levels previously reported in the literature and textbooks concerning malnourished infants who had been cured of their actual disease were not assessed in this environment, but at the customary ward temperature, i.e. under inadequate conditions. Accordingly, such results are not real; they rather reflect the distorted data on the forced adaptation which develops in response to the chronic burden of the aphysiological environment. The comparative experiments assessing the influences of the environmental temperature clearly demonstrated that the physiological milieu for true malnourished infants is the comfort climate at elevated temperature (around 29 °C).

In severe infantile malnutrition the thermoregulation of the vital processes is an important and decisive factor. Recognition of the vital role of a thermoneutral comfort environment shed light on the basic features of the aetiopathogenesis, the pathophysiology and the adaptation mechanism, and revealed the only correct means of quantitative and qualitative feeding for normalization of development.

In contrast with the ramified endogenous conception that had persisted for about a century, it was assumed that the cause of the inability to gain weight was not to be sought exclusively in the endogenous milieu.

From 1951, I was continually occupied with the thoughts that formed the basis of this hypothesis. The essence was as follows: the severe disturbance in weight gain after elimination of the basic and intercurrent

diseases is not a consequence of an exorbitant and aimless breakdown of the tissues or wastage of the nutrients, nor of a complicated metabolism problem. The inability to put on weight (disregarding the significant group of hereditary and acquired systemic diseases) is not maintained by a quantitative or functional hormone or enzyme insufficiency, nor by atrophy of the heart, nor by a deteriorated circulation, nor by a

pathological cell or organ activity, but by a previously not recognized pathophysiological situation.

The development may be inhibited by the customary room temperature of 20–22 °C, an inadequate, cold environment from the aspect of a true malnourished patient. The positive impulse towards this recognition was provided by Kulin's calculations which demonstrated that the usual constant ward temperature of 20–22 °C means a pathologically cold environment for a severely malnourished infant to put on weight. A considerable disparity arises between the surface area and the weight of an infant who does not increase in weight; apart from the surface area/weight disparity, the energy loss is enhanced by the fact that the peripheral heat regulation is in very poor condition. The adipose tissue has already disappeared, or is in the process of disappearing. The total covering surface area is enormously high compared to the body weight. The loss of heat by radiation, conduction and evaporation is enhanced. The intensity of heat emission is also increased by the radius of curvature of the body giving off the heat. In atrophy in such an environment, the failure of the peripheral heat defence system has the consequence that there is such an extensive heat loss from the free skin surfaces and the respiration surface that even warm clothing and an increased total diet together can not eliminate the resulting energy deficit. Well selected protective clothing does moderate the

heat emission from the external surface of the body, but it can not offset the quantity of heat given out via the respiratory system. Engel [4] reported that the body surface area/volume quotient in adult, neonate and premature infants is 0.26, 0.70 and 0.90 cm⁻¹, respectively; in a severely malnourished infant, according to the investigations of Kulin and coworkers, this value is 0.99 cm⁻¹. Having recognized the importance of the energetics of heat emission in the pathology of malnutrition, I realized that the humidity and temperature of the air constantly in contact with the respiratory system are extremely important; it is by no means irrelevant whether the temperature of this external air is 20 °C or 30 °C, for instance. At the customarily applied room temperature, the malnourished infant must devote a large proportion of the chemical energy to maintaining the body temperature. This is the reason why assimilation does not occur [9, 10, 11]. My calculations indicated that in such severely underweight infants the optimum dietary energy requirements are nearly twice the physiological requirement: 180–210 cal/kg/day [12]. The malnourished infant is not capable of the continuous consumption of this amount, which exceeds the maximum tolerance of eutrophic infants (150 cal/kg). Such a forced caloric excess may lead to an unavoidable catastrophe.

About 700 of our cases proved that an environment of around 29 °C, with a relative humidity of 60–70%, guarantee a previously not observed devel-

opment for malnourished and degenerated infants [9, 10, 11, 14, 5, 33]. The serial results confirmed Kulin's earlier assumption from 1952: experience acquired with malnourished infants in the optimal—comfort—climatic milieu permits the conclusion that the basal metabolic level in these cases is strongly dependent on the external temperature.

The pathological state of the body of the malnourished infant results in a disturbance of the equilibrium of the chemical and physical thermoregulation, and leads to a pathological heat turnover. This "pathological" thermoregulation is the consequential reason which, after elimination of the primary and intermediate causes, is responsible alone and without support for the malnourished condition and for the inability to develop. The organism does not build up, for it causes too great a degree of breakdown. The enhanced energy requirement of the malnourished infant can not be met successfully through an increased intake of food. The only realistic solution is to ensure the physiological turnover of the energy by restoring the pathological heat turnover.

As far as the environmental factors are concerned, an appropriate physiological milieu for malnourished infant is attained by elevating the temperature and the humidity; as a consequence, the excessive burn-up of the nutritional and body substances ceases, and the organism utilizes the materials in question for assimilation. The chemical energy released by regulation of the heat turnover is

incorporated into the organism of the malnourished infant, who will therefore put on weight [9, 16, 20].

The effects of the two environments on the weight curves clearly reveal that the temperature is of great importance for the malnourished infant. In many cases it was found that there was a weight stagnation at the usual ward temperature, but a steady weight gain at the 28–30 °C climate, even though the nutrition in the two cases was identical. This is a striking evidence that the conditioning of the environmental air can lead to a decisive effect on the energy turnover and on the equilibrium state of assimilation and dissimulation.

The acute and chronic effects of the climate on the vital functions have been investigated at the Department of Paediatrics in Debrecen since 1952 [22, 29]. In infants suffering from severe malnutrition (decomposition) in the appropriately humidified, air-conditioned climate at 29 °C, we experienced that, sometimes within a few hours, but generally after several days, the passive, motionless, almost lifeless body is reactivated, while the bradycardia, the bradypnoea, the pallid, leaden complexion, the coldness of the extremities and the acrocyanosis usually disappear.

It was also found that, in malnutrition involving a weight deficiency exceeding 25%, the basal metabolism is in general subnormal. Their calculations revealed that the basal metabolism in malnourished infants with a weight deficiency of 33% was about 30% below the physiological

zone. The vast majority of the malnourished infants do not even attempt to attain the physiological basal metabolic level, which is the principal precondition for undisturbed vital functions [16, 29].

The clinical comparative experiments on self-controls at the customary room temperature of 20–22 °C and in the conditioned milieu at 28–30 °C demonstrated that, in response to a period of 48 hours spent in warmer climatic environment, the basal metabolism referred to 1 kg/body weight rose by an average of 12% in the moderately severely malnourished cases, and by 25% in the severely malnourished cases. Their observation that the O₂ consumption is low in an appropriately humidified environment at 22 °C, but rises in the corresponding environment at 28–30 °C, indicates that the basal metabolism in malnourished infants follows the body surface area law in a paradoxical manner [29].

The acceleration and enhancement of the basal metabolism in severe malnutrition is impressive. This suggests that, even in the most apparently hopeless cases of very severe malnutrition, the way is open to the assimilative metabolism.

The neurohormonal/radioiodine assay studies helped in the final clarification of the opposing views that had emerged in connection with the intensity of the basal metabolism.

The investigations on radioiodine excretion and on the iodine bound to the serum proteins quite clearly proved that the reduced function ob-

served in the environment at room temperature (a hypofunctional hypothyroid state) is not irreversible, even in the most severe malnutrition. In the thermoneutral, adequately humidified environment, the hypotrophic infants decrease their thyroid function, in the same way as for the eutrophic infants, whereas the malnourished infants increase and then normalize their thyroid function.

The 17-ketosteroid, metopyrone-test investigations carried out at the clinic confirmed that in malnutrition the subnormal ACTH production found in the environment at room temperature, and also the adrenocortical function, are increased and then normalized by the milieu therapy.

The fact that the activities of the adrenal cortex and the thyroid decrease in inadequate environment, whereas in the same malnourished subjects they increase in the comfort climate, is to be regarded as a consequence of the adequate change in the intensity of pituitary ACTH and TSH production. During the rising activity of the pituitary, thyroid and adrenocortical functions, the subnormal basal metabolism calculated on the basis of unit eutrophic weight corresponding to the length of the malnourished infant, accelerates and then normalizes; the physiological extent of the assimilative metabolism is manifested.

Under comfort climate, the dynamics of the circulation normalizes, the pulse rate and the respiratory rate increase, the arterial and venous blood

pressures improve, the cardiac output rises, the circulation time is shortened, the quantity of blood circulated per unit time increases, and the cardiac performance is elevated by 30%.

The restored O_2 tension conditions set the scene for the restitution of the cells. In conjunction with the change of the circulation conditions in the physiological direction, the absorption improves and the degree of alimentary transport is enhanced; these play a critical role in initiating and continuously ensuring the ability to put on weight. The view of Kulin and coworkers according to which in malnutrition the equilibrium between the circulation and the absorption is upset appears acceptable. It is an everyday experience that a chronic haemodynamic disturbance can inhibit growth and weight gain. They merely have to consider congenital heart disease and the various forms of stunted growth in chronic hypoxaemic states. The unfavourable circulation automatically limits the absorption of the alimentation in the case of proportionate growth, but even more so in the case of a physical disparity. In infants who have been cured of their accompanying disease, i.e. intact malnourished infants, the disturbance in the circulation dynamics means that the rate and intensity of absorption are not sufficient. The absorption is not automatically poor in malnutrition. The absorption of the nutrients through the intestinal wall does not depend on the circulation. With normal enzyme functions for example, there may be an increase

in the permeability of the intestinal wall as the temperature rises, which naturally leads to better resorption.

The protein balance studies performed at the clinic revealed that, after a period of 4–6 weeks in the thermoneutral climate, with almost the constancy of the nitrogen intake, on average there was a considerable decrease in the amount of nitrogen excreted with the faeces and with the urine. These data point to an improving absorption and a favourable assimilation. An increase in the quantity of protoplasm is indicated by the fact that, at the time of a weight increase of 1000 g, the retention of the nitrogen from the food rose by 121%; further, in this period the proportion of the extracellular fluid space on a unit weight basis fell by 20%.

The analytical data on the alpha-amino-nitrogen and the uric acid are also indicative of a high degree of incorporation of the nutrient constituents.

Between the 10th and the 14th day of thermoneutral climatic therapy, there was a considerable moderation in the manifest hypalbuminaemia, the amount of gammaglobulin rose significantly, and the enhancement of the blood proteins exceeded the increase of the plasma volume.

In response to the climate at 29 °C, there is an almost immediate fall in the threatening hypoglycaemia. In 90% of the cases, the blood glucose level rises spontaneously to the normal range.

The increased basal metabolism in the adequate environment is a pre-

condition for true malnourished infants to put on weight.

The comfort milieu at around 29 °C is an indispensable requirement for the rational feeding of malnourished infants [15]; in this climate, the alimentary tolerance is broadened, the appetite improves, and there is an optimum increase in the quantity of food that can be consumed.

It may be observed that, in an environment at 20–22 °C, the greater the weight deficiency, i.e. the more marked the disparity between the body surface area and the body substance, the more subnormal the basal metabolism will be; at the same time, in the given malnourished infants (i.e. with an unchanged body surface area) in an adequately humidified environment at 28–30 °C, the more severe the malnutrition, the more intensively the heat production approaches the physiological zone in a 48-hour acute experiment. This experimental finding permits the conclusion that, in the customary room-temperature (inadequate) environment, the energy turnover follows the Rubner surface area law in a paradox way, because of the pathologically deteriorated body structure. In a cool environment, enhancement of the heat production and maintenance of the equilibrium state of the physiological thermoregulation would need amounts of food and body substances and a quantity of reserve energy which the malnourished infant simply does not possess. It must be assumed that, at the usual room temperature, in the malnourished condition of

malnourished infants, the heat impulses arriving from the external surfaces in contact with the air, from the bare skin surfaces and from the respiratory surfaces are inadequate thermal stimuli in a stage of the loss of the body substance that can be defined well in terms of the weight deficiency percentage (PI) [16, 17].

The malnourished infant does not follow the fundamental law of physiology in the thermal regulation. The basic law of thermal regulation states that the indifferent temperature is a zone of the environmental temperature within which the basal metabolism does not change, but remains at the physiological basal level. In contrast with this, it was found that the neutral temperature of atrophic infants is the higher zone of the environmental temperature in which the subnormal basal metabolism increases suddenly, the intensity of the increase being the more marked, the more severe the malnutrition. In the course of the chronic warm climatic treatment, the basal metabolism approaches and then attains the limit of the normal range for the eutrophic infant and then becomes constant at this level [18, 19].

If we are investigating whether the neuroendocrinological mechanisms regulating the basal metabolism are in harmony in severe malnutrition, then it must be examined whether the decreased function observed in the inadequate climate is pathological or inevitable. For the maintenance of the intensity of the physiological basal metabolism in the constantly cool

environment, a certain quantity of reserve energy is needed which the malnourished infant simply does not possess. If, in this situation, the neuro-hormonal system were to function with the same intensity as in an intact body structure under normal conditions (in eutrophy), it would mechanically follow the body surface area law; consequently, the breakdown and burning-up of the otherwise considerably diminished protoplasm substance would speed up to such an extent that complete degeneration would occur within a matter of days. The basal metabolism falls below the critical level, and is so low that it cannot even maintain the body temperature. In this hypothermic state, the malnourished infant drifts into the end-stage. To avoid this, his organism tenaciously adheres to a "fixed" metabolic situation, which at the same time is the "maintenance" minimum of the basal metabolism. The pituitary does not degenerate irreversibly, but adapts to the needs of the malnourished organism. The vital functions accommodate to this decelerated metabolic intensity. The classical investigators instinctively, but without knowing the internal correlations, aptly referred to the reduced, but "harmonized" function as *vita parva* [22]. The slowed-down vital functions at 22 °C, inadequate climate serve merely to maintain life; at the same time, then inhibit the weight gain and the physiological development. This reduced functioning is an inevitable forced adaptation to the diminished alimentary and body substances.

A logical analysis of the facts made it clear to the author that the broken-down thermal regulation is, in fact, not a pathological state *sui generis*, but a defence mechanism. In the adequate humid milieu (the thermo-neutral climate), the causes and consequences of the disturbance in weight gain are eliminated by the acceleration of the vital functions, by the appropriate quantity of food, and by the real distribution and desirable utilization of the alimentary energy; these factors create the physiological conditions for biological development and weight gain. This turning of the activity of the organism in the physiological direction is a purposeful adaptation. This broad amplitude of adaptation proves that the severely malnourished organism is capable of participating with an imposing degree of efficiency in the regulation of the vital processes [24].

In severe infantile malnutrition, the thermoregulatory adaptational mechanism is closely correlated with the organ systems and the climatic environment.

The pituitary, thyroid, adrenocortical system is a system regulating the economy of the utilization of the energy, i.e. the metabolic intensity corresponding to the requirements. On the basis of the clinical observations and the experimental study of this system, it must be assumed that the chronic cold impulses arriving from the surfaces in contact with the environmental air, the bare skin surface and the respiratory surface, act in a braking manner via the hypo-

thalamus in a well-defined critical stage of the loss of the body substance, influencing the hormonal system regulating the physiological basal metabolism. A change in the environmental temperature acts as a peripheral impulse through the mediation of the thermoreceptors. Through these impulses, the vegetative nervous system economically regulates the functions of the organs and organ systems by hormonal means in severe malnutrition, too [29].

The recognition of the adaptational mechanism opened the way to the understanding of the pathogenesis and pathophysiology involved in severely malnourished infants, and demonstrated the only rational way of alimentation to attain development and weight gain. It became obvious that there is a pathological condition in extremely malnourished infants who have been cured of their actual diseases, due to which their vital functions are slowed down to a state of "vita minima"; in this condition, the thermoneutral climate proved to be an effective therapeutic factor, by normalizing the vital functions of the organs and organ systems [29].

By means of bedside observations and exact experiments, the author and coworkers confirmed that the comfort climate resolves those inhibitory factors which maintain the disturbance of the weight gain. Their comparative clinical and experimental observations on self-controls in the inadequate and adequate environments quite clearly indicate that the cause of the different parameters in

the organism of malnourished infants cured of their actual diseases from the analogous parameters in healthy eutrophic infants with a normal body structure is to be sought in the organic changes and in the pathological functional disturbances. If these differences in function and in the physiological constants were the consequences of similar pathological events, it would hardly be possible to observe that the inability to develop (which is otherwise impossible to influence in the vast majority of the cases) gives way to continuous development in an about-turn manner in many instances merely in response to the adequate climate.

The research which had previously been carried out world-wide had not led to a satisfactory result. My investigations from 1952 on showed that the earlier work had not clarified the essence of infantile malnutrition. A logical interpretation of the results of our research work taking into consideration the scientific requirements had revealed ingenuously that the vital functions in malnutrition are organized by the climatic therapy. This is such a deciding factor that the prospects for life and development of the previously hopeless cases, the infants suffering from severe malnutrition, were improved to an extent that was earlier not dreamed of.

My clinical observations and experimental results have stood the test of time. My experience with the application of the optimum thermoneutral environment of 29 °C in infantile malnutrition has been reported

in virtually all of the scientific world-languages, and has become part of various foreign monographs and textbooks.

Both fundamental detections as pathogenesis, climatic therapy, and particular recognitions, as revealing of pathophysiology, adaptational mechanisms, rational feeding, achieved a respect internationally: Betke K [1], Brooke O G et al [2, 3], Ewerbeck H [5], Iancu A [6, 7], Kleinschmidt H [8], Maslov M S [31], Ponomaryeva P A and Grechishnyikova L V [32], Thurau R [33].

The majority of publications I have written since my retirement have had the aim of confirming my original discoveries relating to infantile malnutrition [20, 21, 22, 23, 24, 25, 26, 27, 28, 29]. Everything has shown that this solution of the earlier problems of curing infantile malnutrition is a correct one.

It is impossible to give a detailed survey, because of the myriad wide-ranging and often contradictory results and data that have accumulated over the years. However, the systematic elucidation of the mechanism of action of thermal regulation and the thermoneutral milieu has demonstrated those factors that aggravate the pathology of the basic process in infantile malnutrition as well as those functions that take place of necessity in the interest of maintaining life and of promoting the development of the body.

Figures 1 to 11 reveal the fates of malnourished infants who had weight deficiencies of 23–30%. The data

given are the energy quotient ($EQ = \text{calorie per kg}$), the body temperature, the weight curve and the development quotient ($DQ = \text{fraction of optimum body weight for age}$). The section to the left of the thick vertical line relates to the time in the climate of 22 °C, while the section to the right of it reflects the period spent at the climate of 28–30 °C.

In Figs 10 and 11, the vertical thick dashed line denotes the commencement of the non-ventilated “semi-conditioning”.

To prove that the excellent effect of the conditioned milieu is not to be ascribed primarily to the ventilation (the elimination of catarrhal and other infections), but rather to the humidity-rich high-temperature atmosphere, some infants were placed in non-ventilated rooms, in which a temperature of 28–30 °C and an appropriate humidity were attained by primitive means. These infants, too, underwent considerable weight gains, as illustrated by cases 20 and 21, in whom there had been a tendency to irreversibly severe malnutrition. Before these cases are discussed, several points must be mentioned.

It is obvious that the “closed”, non-ventilated milieu is not appropriate, because of the danger of volatile infections. Ventilation is an advantageous supplement to the conditions of the cure (by reducing the possibility of droplet infection), but a highly-trained nursing staff and up-to-date care are indispensable.

Figures 10, 11 resp. cases 20, 21 displayed the criteria of severe malnu-

trition. Before case 21, a 3 1/2 month-old infant, was transferred to the climate ward, there was a rapid and extensive weight loss, which exceeded the Quest number. In this case too, entry

into the comfort climate was followed by a continuous weight gain.

As seen in Figs 12-15, the O₂ consumption over a 48-hour period at constant conditioning of 28-30 °C was

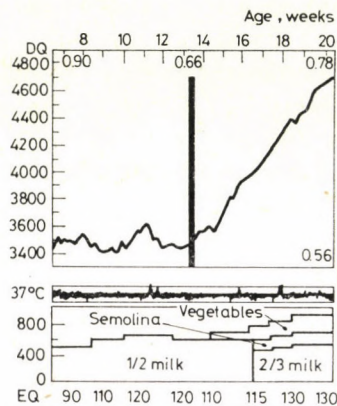


FIG. 1. Case 8. Diseases: hypoalimantation; week 7: bronchitis; week 8: enterocolitis; week 10: mastoiditis, antrotomy l.u., pos.; week 11: enteritis; week 12: bronchiolitis; week 18: bronchitis, otorrhoea. The weight stagnated for 8 weeks. Following the age of 13 weeks, there was a satisfactory development at the comfort climate

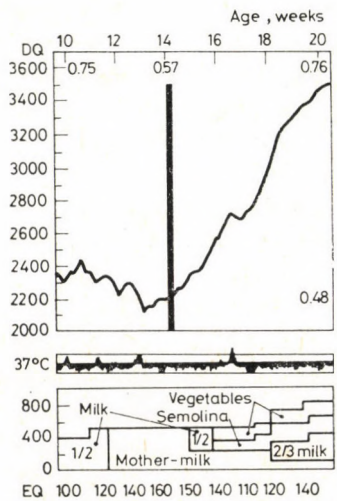


FIG. 2. Case 9. Diseases: week 10: bronchitis, latent otitis; week 11: mastoiditis, antrotomy l.u. pos., thrush; week 12: bronchitis; week 14: bronchiolitis, circulatory failure; week 15: enteritis; week 17: enterocolitis. The duration of weight stagnation (weight fall) was 8 weeks. During 6 weeks at the thermoneutral climate from the age of 14 weeks, the weight gain was 1200 g

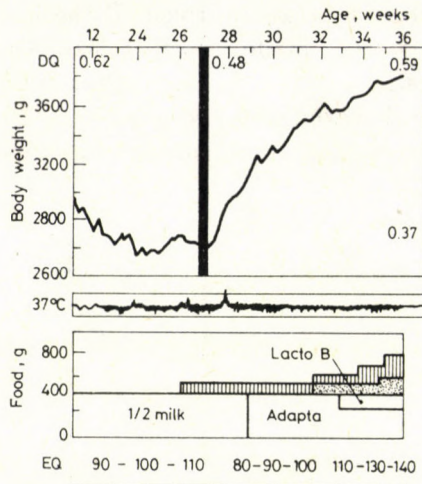


FIG. 3. Case 12. Diseases: week 22: enterocolitis, dehydration; week 23: otitis; week 24: mastoiditis, antrotomy l.d. pos.; weeks 27-28: grippe; week 35: furunculosis, cystopyelitis. The weight gain in the thermoneutral climate was continuous

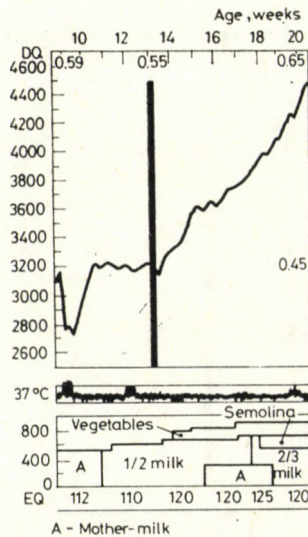


FIG. 4. Case 2. Diseases: the right arm was broken at birth; week 3: enterocolitis; week 5: bronchitis, otitis; week 7: enterocolitis; week 9: dyspepsia coli 0111 infection, diarrhoea, dehydration, which were cured within 10 days. Apart from a transitory temperature rise, transfer into the higher-temperature climate was preceded by a 20-day symptom-free period. For 2 months following the birth the weight had stagnated, but during 6 weeks at 29°C the weight gain was 1300 g and the average rate of weight gain exceeded that for eutrophic counterparts. At home, during the 5 weeks following the discharge, up to the age of 5 months the weight increased from 4500 g to 5550 g, while the DQ rose from 0.65 to 0.73. The monthly weight gain was 900 g. The body length increased by 4 cm, in place of the increase for age of 1.5 cm. The infant remained healthy, with a good appetite

studied, together with comfortable humidity; measurements were made after 0, 24 and 48 hours.

The Figs demonstrate that whereas the 0-hour conditioning scarcely in-

fluenced the heat production, the effect of the 24-hour conditioning resulted in a considerably increased O_2 consumption. The increase after 48 hours was even more marked.

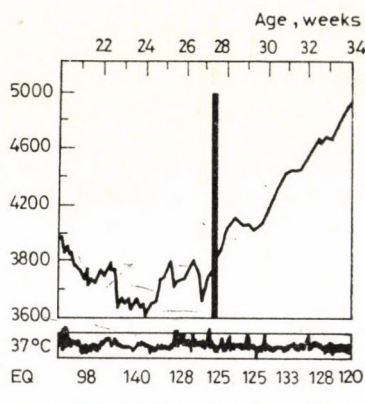


FIG. 5. Case 3. During 4 weeks in the normal-temperature climate after an infectious febrile state, the infant lost 500 g. This was followed by a gain of 200 g, but there was then a further weight loss. A continuous weight gain was not to be expected after the given history and a further febrile period. At the customary ward temperature, the situation appeared risky and hopeless. At the higher-temperature climate, without a restoration interval, there was an immediate weight gain, which amounted to 1200 g in 6 weeks. If the infant had entered the latter climate at the age of 26 weeks, it might have been conceived that the weight was rising in the post-restoration period

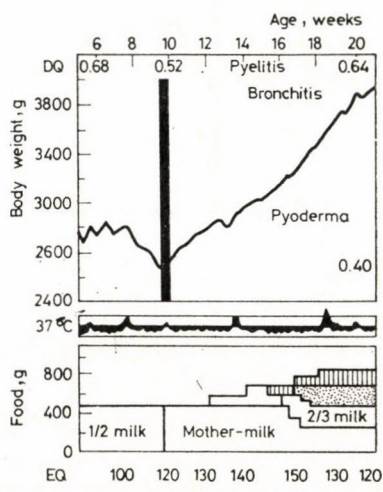


FIG. 6. Case 19. The rapid weight loss of 400 g at inadequate climate was instantly reversed at comfort climate and development commenced at once. The favourable effect was not inhibited by the subsequent bronchitis, pyelitis and pyoderma. During 11 weeks, the weight gain was 1400 g

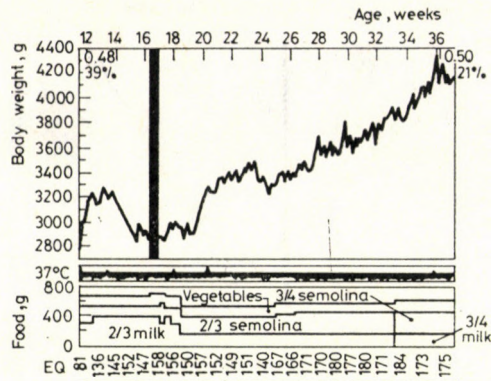


FIG. 7. Case 26. J. Gy., aged 2 1/2 months. In the customary 22 °C ward, he responded to a calorie intake increase with a very severe loss in weight. At comfort climate from the age of 17 weeks, his weight initially stagnated. Then, after a transitional break between the ages of 21 and 24 weeks, his weight gain in response to the burden of the extra calorie load was undisturbed. The weight deficiency fell from 39% to 21%

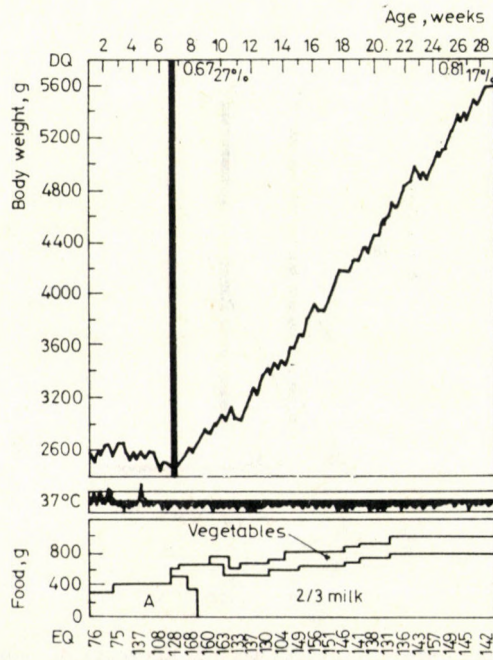


FIG. 8. Case 29. V. P. Admitted after 4 days of high temperature, vomiting and oedema. A picture of chronic sepsis was seen. He recovered slowly and in stages after treatment over 6 weeks. However, there was no development. Following his transfer to the 29 °C conditioned incubator, he immediately began to put on weight steadily. In 20 weeks, his weight deficiency decreased from 27% to 17%

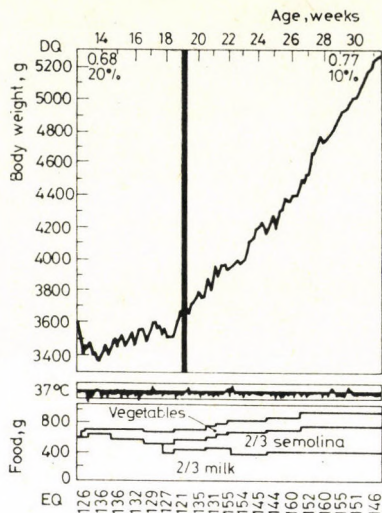


FIG. 9. Case 31. B. S., aged 3 months. Admitted to the 22 °C ward with symptoms of bronchitis, fever and vomiting. He got over the acute disease, but his weight gain in 6 weeks was only 70 g. At comfort climate, his development proceeded satisfactorily. During 12 weeks, the weight deficiency moderated from 20% to 10%, as he gained 1500 g

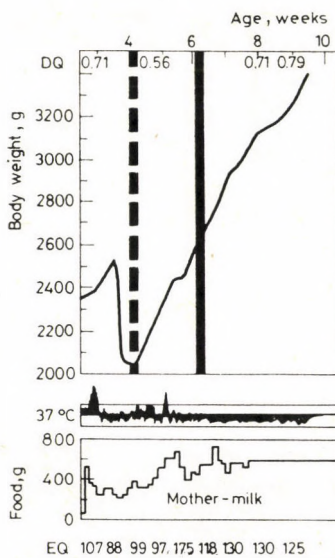


FIG. 10. Case 20. Diseases: forceps delivery; week 2: anorexia, somnolence; week 3: severe enterocolitis, bronchopneumonia, malnutrition. The weight fell considerably after birth. During the semi-conditioning and then the ventilated conditioning, the average monthly weight gain was 1250 g. In the desirable climate and at home, the weight rose from 2000 g to 6500 g in 3 ½ months. The DQ increased from 0.56 to 1.12. The length increase was 11 cm, instead of the increase for age of 5.5 cm. The infant was good-humoured and very lively, and was able to sit on an adult's arm

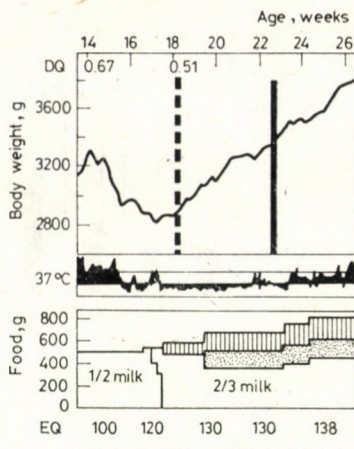


FIG. 11. Case 21. Diseases: since birth the breathing was stridulous and bronchial in nature; week 11: bronchitis, severe enterocolitis, otitis, antrotomy, bilateral antrum empyema, left brachial necrosis; week 15: pneumonia; week 20: furunculosis. Weight stagnation of weight loss for 3 months after the birth

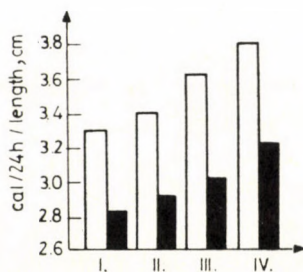
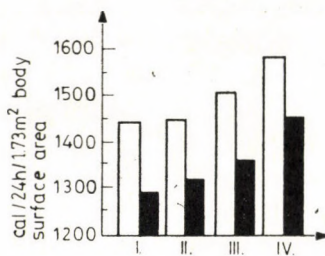
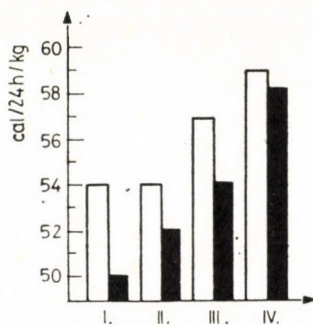
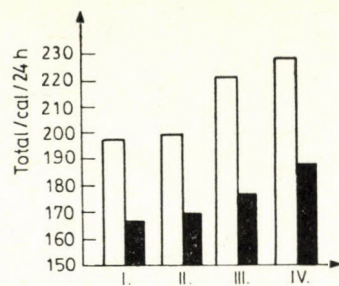
The black columns in Figs 12–15 show that the enhancement of the energy turnover was even more striking in the most severely malnourished cases. The lasting effect of the environmental temperature appears to be a deciding factor in the peripheral (physical) heat regulation of the malnourished infant.

Since each malnourished case served as its own control, the individual differences, i.e. the disturbing effects of the external and internal factors of the body structure, were totally eliminated. As a consequence, it was virtually unimportant whether the O_2 consumption was referred to the surface area, the weight or the length of the body. No matter which body unit was taken as the basis of reference the direction of the intensity of the energy turnover in response to the climatic change was the same.

Much research has been carried out on the basal metabolism of malnour-

ished infants. I considered that the solution of the very disputed problem of the data obtained did not depend exclusively on the careful selection of the patients to be examined, the application of ever better technical methods and the results we published, but also on a comparative analysis of the basal metabolism and neurohormonal values found under fixed experimental conditions.

Figure 16 gives the mean 24-hour values for the excretion of ^{131}I in the urine from eutrophic, mildly malnourished and more severely malnourished infants after acclimatization at the customary room temperature of 20–22 °C, and after a period of 2 months in an appropriately humidified climate at 28–30 °C. The Fig. reveals that, in response to the humid, warm climate, the mildly malnourished infants behave in the same way as the eutrophic infants, whereas the truly malnourished infants behave differ-



FIGS 12–15. Effects of an air-exchange, comfortably humidified climatic environment at 28–30 °C on the heat production of malnourished infants

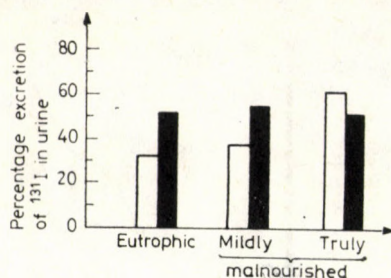


FIG. 16. Average 24-hour excretion of ^{131}I in the urine from eutrophic, mildly malnourished and truly malnourished infants at a room temperature of 20–22 °C (empty columns) and after a period of 2 months in a comfortably humidified, air-exchange atmosphere at 28–30 °C (black columns)

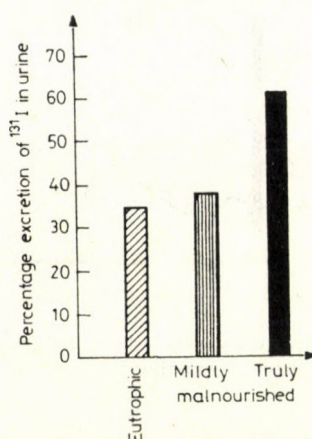


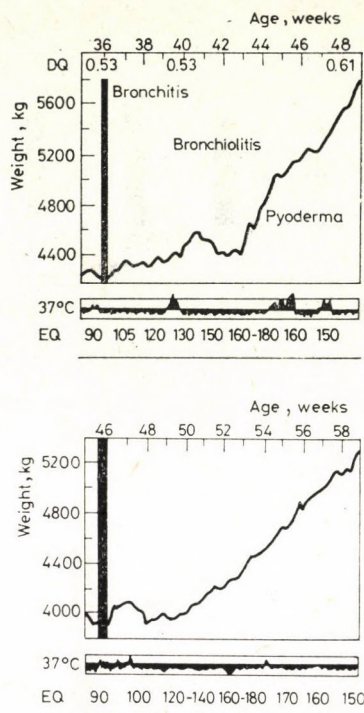
FIG. 17. Average 24-hour excretion of ^{131}I in the urine from eutrophic, mildly malnourished and more severely malnourished infants in an environment at 20–22 °C

ently. From a comparison of the final pair of columns in Fig. 16 with Figs 12–15, it may be stated that the warm climate affects the basal metabolism and iodine exchange of atrophic infants in the same direction.

Figure 17 depicts the average 24-hour excretion of ^{131}I in the urine from infants in an environment at the customary room temperature. It can be seen that the thyroid of the malnourished infants stores about 80% less iodine than the thyroid in mildly malnourished infants, and

about by 90% less iodine than that in the eutrophic controls. Figure 17 confirms the correctness of our earlier finding that, no matter what the body unit to which the O_2 consumption is referred (the body surface area, the weight, or the ideal weight corresponding to the length), the basal metabolism in malnourished infants is low relative to that in either eutrophic or mildly malnourished infants.

The excretion of 17-ketosteroids was studied in adequate and in in-



FIGS 18, 19. Cases 35 and 36. Two older malnourished infants who put on weight to the accompaniment of an excellent alimentary tolerance

adequate climatic environments in infantile malnutrition. The clearly low 17-ketosteroid excretion at the inadequate (20–22 °C) environmental temperature underwent a significant enhancement in the thermoneutral climate (generally rising by a factor of 2, or even 3).

We explain the ability of the 17-ketosteroid excretion to rise in the comfortably humidified environment at 29 °C, and to remain lasting at a normal level, in terms of the intactness of the ACTH-adrenocortex axis; support was lent to this by the result of our ACTH reserve studies to date.

All textbooks earlier stated quite definitely that the optimum caloric

needs of an infant decrease from 120 cal/kg/day in the first few weeks of life to 70 cal/kg/day by the end of the first year. The experience I acquired from the use of the climatic milieu convinced me that the physiological restriction of the alimentary capacity is only apparently dependent on the age; in fact, it is dependent on the physical development and the biological maturity. This is confirmed by the fact that the optimum nutritional uptake in malnourished infants treated in the adequate climate was rarely less than 120 cal/kg/day, independently of whether the infant was 6–8 weeks of age or much older (8–12 months). If the energy needs were

a function of the age and not of the biological maturity, the older malnourished infant would not put on weight even in the thermoneutral climate.

Thanks to this directed adaptation, in the climate the older malnourished infant too is able to consume and utilize a considerable quantity of food, in an undisturbed way, without undergoing any harm.

29 of our cases displayed a gain in weight at an actual calorie intake excess of 10–30 cal/kg/day. To illustrate the therapeutic effect, Figs 18, 19, cases 35 and 36 were outstanding examples of subjects with an imposing alimentary capacity who were kept in the climate. This broad range of alimentary capacity is a feature of the intact metabolic function. However, the ability of the organs of a severely malnourished infant to function is revealed only in the thermoneutral environment. The paradoxical negative responses frequently observed in the customary milieu did not ensue in a single case in the thermoneutral

climate, in spite of the immense quantities of food.

If the heat production is followed in Fig. 20 as a function of the weight deficiency, it is seen that, at the customary room temperature (column I for the various groups), from a certain point (group 3) the average heat production falls below the eutrophic level, and that, with increase of the percentage weight deficiency (groups 3–7) at room temperature (column I), the heat production gradually diminishes. The heat production of the severely malnourished cases (groups 6 and 7) at room temperature is well below the normal range. It is noteworthy that the individuals in group 1, with a relatively insignificant average weight deficiency of 5%, displayed very considerably differing weight gain indices: 46–103. As concerns the heat production, however, they behaved like the eutrophic infants. In response to 24 hours in the warm climate, their energy turnovers decreased to the maximum extent

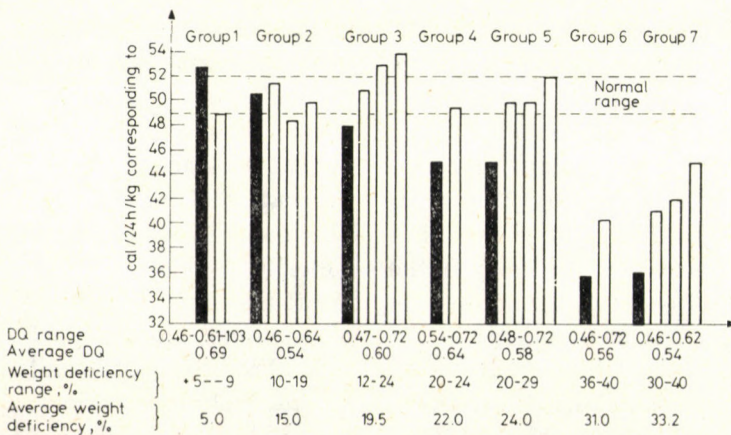


FIG. 20

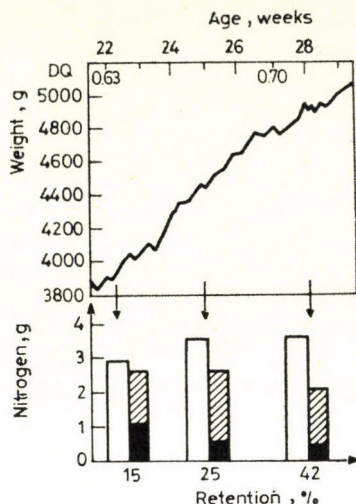


FIG. 21. The uniformly increasing nitrogen incorporation is followed by a satisfactory continuous gain in weight in the comfort climate

within the physiological limit. In group 2 (individuals with a weight deficiency of 10–19%, on average 15%), the heat production in the warm climate did not differ from the normal value measured at room temperature. In the individuals in groups 3–7, the heat production was always elevated intensively, roughly in parallel with the percentage increase in the weight deficiency, after 0 hours (II), 24 hours (III) or 48 hours (IV) in the climate. The heat production in group 7 (average weight deficiency 33.2%) started from a low value, and had progressively increased by 25% after 48 hours. The Fig. also shows that the larger the weight deficiency in the 20–22 °C environment, the more subnormal the basal metabolism; in the same malnourished infants at 29 °C, appropriately humidified environment, the more severe the malnutrition, the more intensively the heat

production approaches the physiological zone in the 48-hour acute experiment. The detailed data are to be found in Table III of the monography.

Figures 21, 22, in each pair of columns, the blank column gives the amount of nitrogen consumed, while the shaded and the black part of the adjacent column show the amounts of nitrogen excreted in the urine and in the faeces, respectively.

As concerns the case history of the malnourished infant with Leiners disease, it should be stated that this patient was admitted to the climate ward at 22 °C at the age of 7 weeks. The cutan lesions responded satisfactorily to local and general treatment. However, in spite of a series of plasma and blood transfusions, the general condition of the infant became progressively more serious, and the incessant loss of weight led inexorably towards very severe malnutrition.

At the age of 11 weeks, the infant was transferred to the thermoneutral climate. Nitrogen balance examinations at that time revealed a very low retention. The high contribution of the faecal nitrogen to the total nitrogen excretion was striking. When the second series of measurements were made, the protein consumption has doubled, whereas there was no change in the nitrogen retention, because of the considerable excretion. However, there was a substantial alteration in the proportions of nitrogen excreted in the faeces and in the urine. The improved nitrogen utilization was accompanied by the commencement of weight gain (Fig. 22). Between the ages of 7 and 11 weeks, our Leiner's disease patient lost 900 g in the customary ward milieu. In such an environment, we could have little hope not only as regards weight gain, but also for survival. Nevertheless, the transfer to the thermoneutral climate was accompanied by the dramatic and immediate cessation of the rapid and

apparently fatal loss in weight. Following this, despite the severe metabolic disturbance, there was a tendency (admittedly a slow one) towards a gain in weight. In parallel with the restoration of the protein metabolism (nitrogen balance), there was a weight gain of 1300 g between the ages of 22 and 30 weeks; this can be said to be an ideal development.

It was found in several patients that, after healing of the dermal phenomena in the cases of malnutrition associated with Leiner's disease, the improvement of the protein incorporation was inhibited for various periods by the metabolic disturbance involved.

When we discovered that, at the time when our malnourished infants exhibited a weight gain of 20–30%, the amount of retained nitrogen was more than doubled relative to the initial level, it was apparent that the nitrogen breakdown had been replaced by nitrogen incorporation. In every case, the nitrogen retention per kg

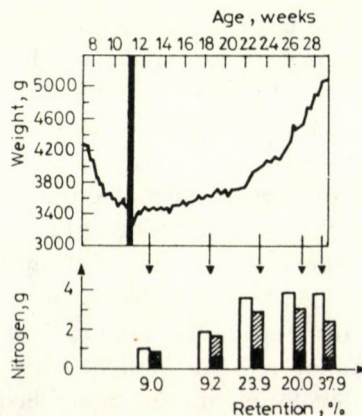


FIG. 22. The change in protein incorporation in the comfort climate following the metabolic disturbance accompanying Leiner's disease

body weight rose in this climate, often by a factor of 2-4 times (e.g. Fig. 22).

It may be seen that, in response to treatment in the thermoneutral environment for 6-8 weeks, which resulted in an average weight gain of 1000 g, the nitrogen retention increased by 121%. The extent of the improvement in the retention varied from case to case: in general, the lower the initial retention level and the greater the extent of the malnutrition, the more striking the improvement was.

It is not surprising that, at the end of climatic treatment for 7 weeks, after an appreciable gain in weight, i.e. when the infant is already mildly malnourished, the nitrogen consumption per kg body weight is less than at the beginning of treatment. The essence is always the same: if the infant develops nicely, then he utilizes a sufficient quantity, even if there are fluctuations in the individual phases of weight gain. Overall, every infant organism incorporates as much protein as is possible in the given situation, and as much as necessary in the various stages of development. What is the explanation (Kulin and Ludmány 1957) of the fact, that, at thermoneutral climate, some of the malnourished infants developed twice of the normal average tempo (1000 g per month; e.g. Fig. 21) with half nitrogen retention (30-35%)? No matter how we evaluate our data, we cannot reduce the complex processes of development of malnourished infants to a single numerical parameter. Even at the end

of the climatic treatment, our malnourished patients had not attained the retention levels characteristic of eutrophic infants. When the malnourished infant has put on appreciable weight in the climatic environment, he is still only mildly malnourished (hypotrophic). Accordingly, the various parameters relating to the body development (including the nitrogen retention) are not necessarily the same as in the eutrophic case.

The reason why we were the first who were able to carry out series of nitrogen-balance examinations on malnourished infants who were putting on weight is due primarily to the fact that truly malnourished infants only exceptionally demonstrated a weight gain in any country at that time. Following the introduction of the application of the thermoneutral climate, we had abundant material allowing us to follow the protein utilization both during weight stagnation in an inadequate climate and during the various stages of weight gain in the comfort climate.

Figures 23 and 24 depict the circulating blood protein values calculated on an actual weight basis and on the basis of the desirable weight corresponding to the length of the malnourished infant, respectively. These Figs again draw attention to the fact that it is preferable to refer the parameters not to the actual weight, but rather to the average weight corresponding to the length of malnourished infants. A comparison of these two Figs reveals that the data in Fig. 24 approximate much

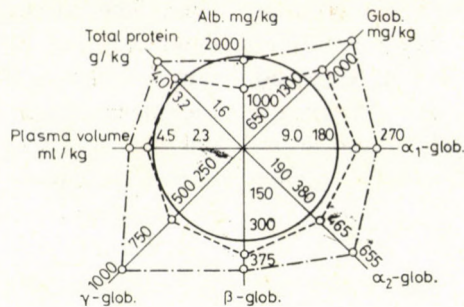


FIG. 23. Circulating protein values referred to the actual weights of the malnourished infants, before climatic treatment (— — —) and after treatment in the thermoneutral environment for 10–14 days (.—.—.). The normal values are shown by the circle

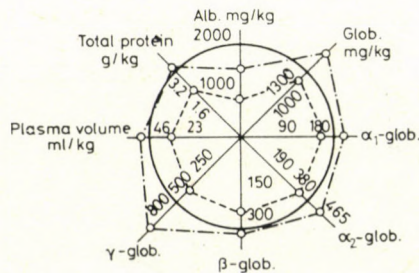


FIG. 24. Circulating protein values referred to the average weight corresponding to the length of the malnourished infants, before climatic treatment (— — —), and after treatment in the thermoneutral environment for 10–14 days (.—.—.). The normal values are shown by the circle

more closely the real situation. The normal values are denoted by the circle drawn in a continuous line; the data relating to a room-temperature of 20–22 °C are denoted by a dashed line (— — —); and the data relating to the thermoneutral climate at 28–30 °C are denoted by a line consisting of alternating dots and dashes (.—.—.). In a clockwise direction (starting at 9 o'clock), the diagrams present data on the plasma volume, the total protein, the albumin, the globulin, the α₁-globulin, the α₂-globulin, the beta-globulin and the gamma-globulin.

These studies were carried out after 10–14 days in the warm environment. Within this time, both in the cases who had put on weight and in those of who had not yet done so, there were clear increases in the plasma volume and the circulating total protein, the manifest circulatory hypalbuminaemia had disappeared or moderated significantly, the amount of gamma-globulin had increased considerably, and the blood protein production was enhanced.

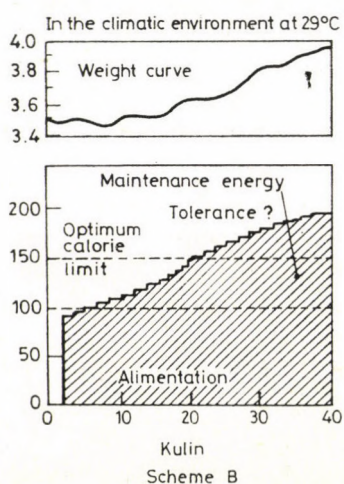
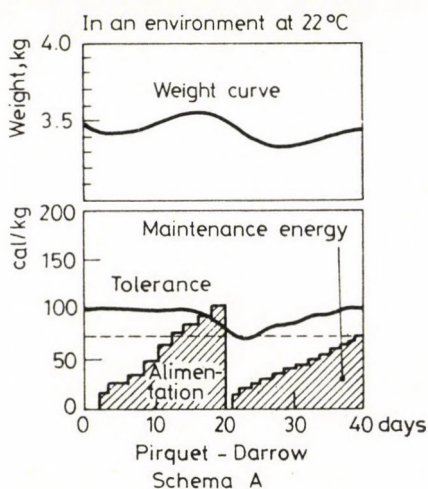
The cause of the reductions in the circulating plasma and protein at the customary room temperature is that

the blood participating in the circulation adapts to the low energy turnover and therefore circulates at a decreased rate; part of the plasma stagnates in the blood storage sites, and some of its properties serve possibly other purposes.

In the humid, warm milieu, the previously inactively "stored" plasma is driven into the accelerated circulation following the rising energy turn-

over. The intensive plasma replacement is also followed by plasma protein formation. The redistribution of the plasma and blood proteins contributes significantly to the resolution of the disturbance in weight gain, and to the development of physiological assimilation.

It is seen, therefore, that, in response to the warm environment in the initial stages after transfer to the



Schemes A and B: Alimentary tolerance in infantile malnutrition

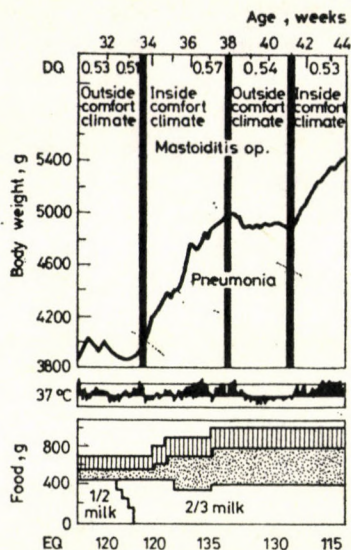


FIG. 25. Case 37. Diseases: week 9: pneumonia; week 11: otitis; week 14: mastoiditis, bilateral antrotomy; week 31: malnutrition, pneumonia, otorrhoea. At this stage he was admitted to the non-climatized ward of our clinic. In week 34, on the day on his transfer to the comfort climate, reantrotomy; osteomyelitis and pneumonia migrans developed, and persisted for 2 1/2 months. This infant, who received the same diet in the same amount per kg body weight in the room-temperature ward and in the thermoneutral climate, suffered from a series of intercurrent infections

thermoneutral climate, both types of proteins undergo an increase. The quantity of blood protein is almost completely normalized, but the physiological ratio of the albumin and globulin is still far from being established. At the beginning of the climatic treatment, the serum proteins with the two different dispersities do not accumulate to the same extent. The increase in the more finely-dispersed albumin in response to the warm environment is by 22% greater than that in the total globulin. This is clearly correlated with the fact that the albumin is formed and reformed at a much higher rate than in the case of globulin.

The Pirquet-Darrow scheme re-

veals the alimentary tolerance as well as the weight curve of malnourished infants cared at a customary ward temperature, while Kulin's scheme shows these data of atrophic infants cared in thermoneutral comfort climate. On the graph of scheme A it is perceivable that, in malnutrition 100 cal pro kg/body weight leads to tolerance exceeding. In contrast, from the corresponding graph in scheme B it is obvious that, in comfort climate, this situation does not attain the tolerance limit of 200 cal/kg. However, my "biological" energy calculations [12] demonstrated that 150 cal/kg in extreme malnutrition roughly corresponds to the 120 EQ value of eutrophics. If the upper limit of tolerance in eutrophy is

150 cal/kg/day, then, on the basis of the principle of equivalence, the upper limit of tolerance in malnutrition in the thermoneutral climate is 180–200 cal/kg/day. In 91% of our malnourished cases, the alimentation ensuring the optimum increase in weight in the comfort climate was 120–150 cal/kg/day, while in 75% of them it was 130–150 cal/kg/day. In this milieu, I experienced that the maintenance alimentation level in malnourished infants who had lost a high proportion of their inactive body substances was not 70–80 cal/kg pro day as in eutrophy, but around 100 cal/kg/day.

Similarly to other cases, when Fig. 25, case 37 was transferred to the thermoneutral climate at 29 °C, he did not wait for the “restitution phase” to occur, but immediately began to put on weight continuously. In spite of the protracted pneumonia migrans and the other diseases persisting for 2 ½ months, in one month he gained 900 g. When he was returned to the ward at 20–22 °C, his weight curve displayed a temporary fall and then stagnated throughout his stay there (3 weeks). When he was again transferred to the comfort climate, on exactly the same amount of the same diet, the course of his weight curve again became ideal. Attention should be paid how the weight and temperature curves developed at the customary room temperature of 20–22 °C and in the comfortably humidified thermoneutral milieu at 28–30 °C. It is by no means a waste of time to reflect on the perfect regulatory mechanism that the emaciated infant puts into

action, presumably in response to the environment at room temperature, in the interest of energy economy.

This observation from our clinical experience is a valuable example demonstrating that the metabolic inversion of the malnourished organism, the pathological thermal regulation, is, in fact, a necessary adaptation to the cold environment. While alternating between the comfort climate and the inadequate milieu (for 2–3-week-periods) on several occasions, the infant was for several months in a febrile malnourished condition; whenever he was returned to room temperature, his weight stagnated or decreased, but when back in the thermoneutral climate he repeatedly and systematically put on weight in a desirable manner. The fever disappeared at room temperature, and repeatedly returned in the warm climate. The intensity of the metabolism was utilized in an economical way at the changed environmental temperature. When he was constrained to a dissimilative metabolism at inadequate environment, the febrile heat production ceased, but the fever was again possible when the predominance of the assimilative metabolism was restored in the thermoneutral environment.

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