PHYSIOLOGY OF PREMATURITY

TRANSACTIONS OF THE FOURTH CONFERENCE
MARCH 25, 26 and 27, 1959

CONTENTS

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March 25, 26, and 27, 1959, Princeton, N. J.

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Fourth Conference on Physiology of Prematurity

THE JOSIAH MACY, JR. FOUNDATION CONFERENCE PROGRAM

DURING THE PAST fifteen years the Josiah Macy, Jr. Foundation has organized more than twenty conference groups, each group meeting for at least two days annually over a period of five or more years. Each meeting is limited to twenty-five participants (members and guests), selected to represent a multidiscipline approach to some urgent problem in the field of medicine and health. The goal of this conference program is the promotion of communication, the exchange of ideas, and the stimulation of creativity among the participants. The purpose of the publication of the Transactions of the meetings is to share, as far as possible, the conference process with a larger audience than could participate personally in the discussions.

These conferences provide an opportunity for informal give and take among the participants. To further this purpose, the number of presentations planned for each day is generally restricted to one or two. The member, or guest, selected to give such a presentation is requested not to "read a paper," but rather to highlight, in an informal manner, some of the more interesting aspects of his or her research, with the expectation that there will be frequent interruptions by participants in the form of questions, criticism, or comment. Such interruptions during the course of a presentation are encouraged and form an essential part of the "group interchange."

The conference program has always been viewed by the Foundation as an experiment in communication in which there is room for improvement and need for frequent reappraisal. Sufficient experience has already been gained to justify the conclusion that this type of conference is an effective way of improving understanding among scientists in medicine and allied disciplines, for broadening perspectives, of changing attitudes and of overcoming prejudices. The further conclusion has been reached, as the result of this experiment, that a major obstruction to understanding among scientists lies in the resistance of human attitudes to change, rather than in difficulties of technical comprehension. Less extensive experience with non-scientists has indicated that the effectiveness of this type of conference is not limited to groups of scientists, but will function in any group meeting where more effective communica-

tion is the primary goal. It is also clear that the same conference technique, with minor changes, is readily adapted to small international conferences.

The style of publication of the Transactions has aroused considerable interest and some criticism. The criticism has been directed primarily to editorial permissiveness which has allowed in the final text, in some instances, too many questions, remarks, or comments which, although perhaps useful during a heated discussion, seem out of context and interrupt the sequence of thought. A few have objected to the principle of publishing in this style and would prefer a depersonalized summary without interruptions.

The Foundation Staff and the Scientific Editors of these volumes welcome criticism and hope to profit thereby in increasing the usefulness of the Transactions to scientists in this country and abroad.

FRANK FREMONT-SMITH, M.D.
Medical Director

HEAT REGULATION

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Levine: I have been asked by our Chairman, Dr. Smith, to introduce the subject of heat regulation by citing briefly some of the older work that was done at The New York Hospital-Cornell Medical Center, principally by Dr. Harry Gordon (14) and Dr. Richard Day (10), with the assistance of Dr. James Hardy.

Body temperature is a function of heat production, heat storage, and heat loss. When the heat production exactly equals the heat loss, the body temperature remains uniform, but when heat balance fluctuates in either direction, either hypothermia or hyperthermia results. The instability of body temperature regulation in the premature infant is caused by alterations in both sides of the equation. When the premature infant is exposed to cold air, heat loss exceeds heat production and he develops a subnormal temperature. Conversely, when the infant is subjected to heat, heat production exceeds heat loss and he develops a fever.

Figure 1 shows that under ordinary conditions the heat production of the premature infant is lower than that of the full-term infant. Under sleeping conditions, the average metabolism of the premature and the full-term infant is approximately the same, about 60 cal./kg./24 hr. However, the total daily catabolism, including both sleeping and wakeful periods (but excluding fecal losses), is lowered in the premature infant; the activity quota in these infants averages around 10 cal./kg., whereas in the full-term infant the activity quota averages around 20 cal./kg. The difference in this activity quota is readily

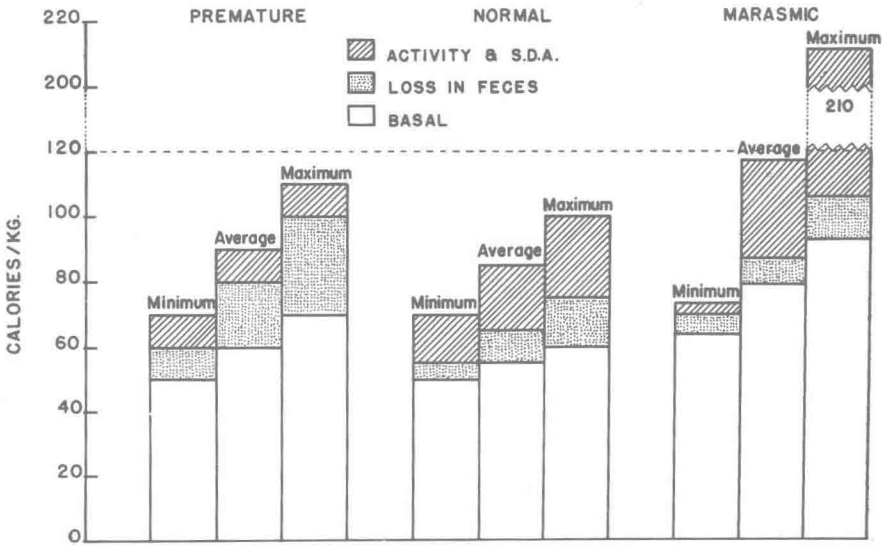

FIGURE 1. Approximate energy expenditure of normal, premature, and marasmic infants. Reprinted, by permission, from Gordon, H. H., and Levine, S. Z.: The metabolic basis for the individual feeding of infants, premature and full-term. *J. Pediat.* **25**, *464-475 (1944).*

explained by the fewer hours of wakefulness and the lower heat production during wakeful periods of the premature infant, the latter being the result of bodily inactivity and feeble musculature.

Table I shows the average figures that Gordon (14) obtained for the total 24-hour catabolism of premature and full-term infants who had been placed in a respiration chamber for 20 or 21.5 hours out of 24. The total daily metabolism of the premature infants, excluding heat loss in stool but including activity and specific dynamic of food, ranged around 70 cal./kg., or 20 per cent above the basal level. In contrast, full-term infants showed a daily maintenance metabolism of about 82 cal./kg., or 40 per cent above the basal. Thus, one of the factors involved in the instability of the body temperature of premature infants is their low total heat production.

In the face of this low total heat production, the premature infant, under comparable cool environments, loses more heat from his body by radiation and conduction than the full-term baby because of a relatively larger surface area and a paucity of subcutaneous insulating fat. The ratio of body surface to body mass in a premature infant weighing 2 kg. is three times the ratio of an adult weighing 60 kg.,

TABLE I

Total Catabolism of Premature Infants

Subject	No. of Days	Average Weight (kg)	Cal/kg/24 hr
C	9	1.8	61
B	24	2.1	70
L	20	2.1	63
O	12	2.1	63
E	9	2.2	73
M	11	2.3	72
C	11	2.4	74
P	9	2.6	65
O	9	2.6	70
L	10	2.7	77
Total	124	—	—
Average	—	2.3	69 (19 per cent above basal)
Full term	—	—	82 (40 per cent above basal)

and virtually three-quarters of his total body mass is within 1 cm. of the surface.

This inverse ratio of heat-producing tissue and surface area is evident when one compares the metabolic rate calculated in terms of body weight and surface area for premature and full-term infants (27). The dotted lines in Figure 2 represent data obtained by Talbot (38);

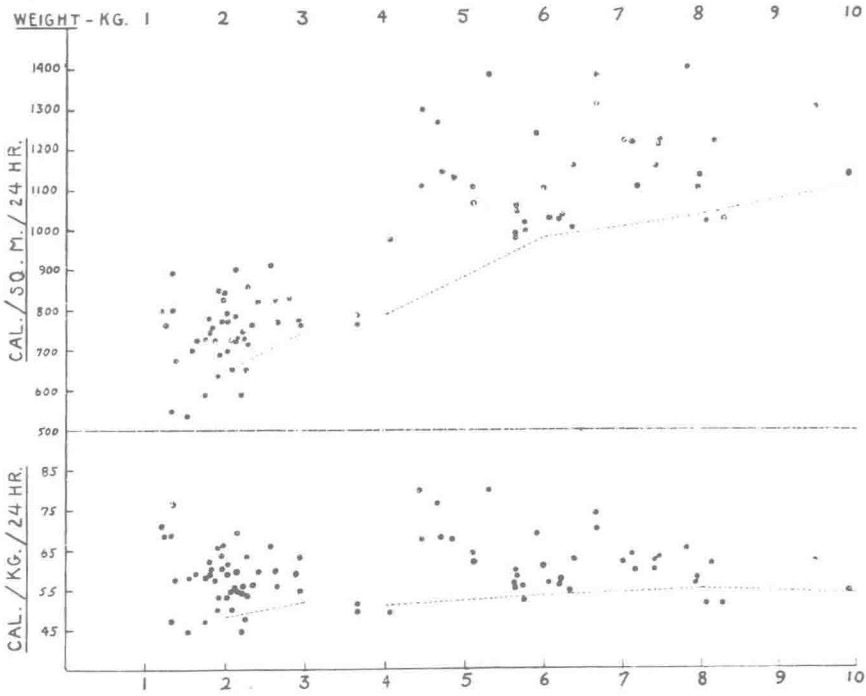

FIGURE 2. Basal heat production of premature and full-term infants in terms of weight and surface area. Each dot denotes a single measurement. The dotted line shows the normal curve. Reprinted, by permission, from Levine, S. Z., and Gordon, H. H.: Physiologic handicaps of the premature infant; their pathogenesis. *Am. J. Dis. Child.* 64, *274-296 (1942).*

the large dots are individual observations obtained in premature and full-term infants in our laboratory. The basal metabolism, when expressed on a weight basis, was roughly the same in premature infants with weights of 3 kg. and under and in full-term infants with weights of 4 to 10 kg., in Talbot's observations. Our observations were at a higher level, but the basal metabolism was again roughly the same in the premature and the full-term infant. But when measurements were based on surface area, there was a significantly higher production of heat in the heavier, full-term infants than in the premature infants.

Reynolds: How did you measure surface area in premature and full-term infants?

Levine: We used the Scammon-Klein (24) formula.

Boell: These curves indicate that the problem confronting the premature infant also confronts the small full-term infant.

Levine: That is correct; these findings are based almost entirely on physical principles and are not related to defective homeostatic mechanisms. These are another problem, but even if there were no defects, the small infant, whether premature or full-term, has more difficulty in maintaining his body temperature than does the larger infant, particularly when he is exposed to environmental temperatures which are below his body temperature. These figures are based on radiation, conduction, and loss. With less than 5 per cent of his total body in the form of subcutaneous fat and with a highly vascular skin, the readiness with which the premature infant loses heat from his body by radiation and conduction is easily appreciated. This would hold true for any small baby.

With the aid of Dr. Hardy, Dr. Day converted our respiration chamber for premature infants into a direct calorimeter and conducted a quantitative study of the factors concerned in heat regulation, that is, heat production, heat loss by radiation and conduction, heat loss by evaporation, rectal temperature, skin temperature, and bodily activity, all observed concurrently.

He was able to demonstrate an augmented heat loss from the skin of the premature infant exposed to cold air. This increase was attributable in part to an increased heat production. In contrast, adults do not show an increased heat production in cool air unless they shiver or have a chill. In the absence of increased muscular activity, an adult will not increase his heat production in response to comfortable cooling. The premature infant, on the other hand, in the absence of overt shivering, which he never does, will increase his heat production. He does this principally by crying and in part by the increased thermal conductivity of his tissues. He has a smaller mass to go through and he is highly vascularized, so that he has an increased conductance of heat from the internal core of his body to the skin, as demonstrated by actual measurements which I will show now. Dr. Day compared his results with those which Dr. Hardy and Dr. DuBois (11) obtained in adults (Figure 3). Thermal conductance means the calories lost from the body based on the difference between rectal and skin temperature per square meter per hour. At all air temperatures, the thermal conductance of the tissues of the premature infant, in seventeen of twenty-one infants, exceeded that of the adults, indicating that heat leaves the internal core of the body of the premature infant with greater readiness and that the skin temperature is higher in relation to the rectal temperature than in adults. The two factors involved are the diminished subcutaneous fat and the larger surface area of the pre-