6. Caldwell FT, Jr. Energy metabolism following thermal injury. Arch Surg 1976; 111:181–85.
7. Caldwell FT, Jr, Hammel HT, Dolan F. A calorimeter for simultaneous determination of heat production and heat loss in the rat. J Appl Physiol 1966; 21:1665–71.
8. Cope O, Nardi GL, Quijano M, et al. Metabolic rate and thyroid function following acute thermal trauma in man. Ann Surg 1953; 137:165–74.
9. Danielsson U, Arturson G, Wennberg L. Variations of metabolic rate in burned patients as a result of the injury and the care. Burns 1978; 5:169–73.
10. DuBois EF. The basal metabolism in fever. JAMA 1921; 77: 352–55.
11. Fisher RA. Statistical Methods for Research Workers. Riverside, Hafner Press. 1970. p. 140.
12. Gagge AP, Burton AC, Bazett HC. A practical system of units for the description of the heat exchange of man with his environment. Science 1941; 94:428–30.
13. Goldenberg M. Adrenal medullary function. Am J Med 1951; 10:627–41.
14. Hardy JD. Fever and thermogenesis. Isr J Med Sci 1976; 12: 942–50.
15. Hardy JD, DuBois EF. The technic of measuring radiation and convection. J Nutr 1938; 15:461–75.
16. Hardy JD, Stolwijk JAJ, Gagge Pharo A. Man. *In* Comparative Physiology of Thermoregulation, Vol. 2. New York, Academic Press Inc. 1971. p. 338.
17. Kleiber M. *The Fire of Life*. New York: Wiley, 1961:132.
18. Liljedahl SO, Lamke LO, Jonsson CE, Nordstrom H, Nylen B. Warm dry air treatment of 345 patients with burns exceeding 20 percent of the body surface. Scan J Plast Reconstr Surg 1979; 13:205–10.
19. Lister G, Hoffman JIE, Rudolph AM. Oxygen uptake in infants and children: a simple method for measurement. Pediatrics 1974; 53:656–62.
20. Neely WA, Petro AB, Holloman GH, Rushton FW, Turner MD, Hardy JD. Researches on the cause of burn hypermetabolism. Ann Surg 1974; 179:291–94.
21. Schmidt-Nielson K. *Desert Animals; Physiological Problems of Heat and Water*. London: Oxford University Press, 1964:17.
22. Schmidt-Nielson K, Crawford EC Jr, Newsome AE, Rawson KS, Hammel HT. Metabolic rate of camels: effect of body temperature and dehydration. Am J Physiol 1967; 212:341–46.
23. Stitt JT. Fever versus hyperthermia. Federation Proc 1979; 38:39–43.
24. Stolwijk JAJ, Hardy JD. Partitional calorimetric studies of responses of man to thermal transients. J Appl Physiol 1966; 21:967–77.
25. Wilmore DW, Long JM, Mason AD, Skreen RW, Pruitt BA. Catecholamines: mediator of the hypermetabolic response to thermal injury. Ann Surg 1974; 180:653–69.

Discussion

DR. WILLIAM A. NEELY (Jackson, Mississippi): Dr. Caldwell has shown without doubt that there is hypermetabolism in burn patients. These slides from our previous study demonstrate again what Dr. Caldwell has shown.

(slide) Please note that this burn patient was hypermetabolic, almost two times normal; this is the normal range. And this is covered, and this is uncovered. Please note that there is tremendous hypermetabolism in the patient uncovered, and all this returns to normal when the patient is grafted.

(slide) The temperature at the time of the study is shown here, in bar graphs. You see that all these differences are statistically significant by the standard deviation.

(slide) This slide shows exactly the same thing, (slide) as does this slide. You will notice that in some of these studies the temperature of the patient was normal.

You will note that the burn patients are particularly hypermetabolic; that this is not abolished when the patient is covered, thus preventing evaporative water loss. I'm sure Dr. Caldwell will say our occlusive dressing would not prevent heat loss, but I will say that I was comfortable in the plastic material that we have put over these patients. And this hypermetabolism does not return to normal until the patient's skin is grafted.

One of these patients, as I mentioned earlier, did not have any temperature elevation in his entire course. This is, of course, rare, but still demonstrates that the patient is still hypermetabolic, even with a normal temperature. There is no doubt that this hypermetabolism is related to both injury and water loss, the latter preventable.

For eons, animals have been covering injury without the benefit of metabolic interference. The question at hand is whether hypermetabolism is favorable, or is an unfavorable reaction to injury, and should we, perhaps, interfere metabolically?

DR. WILLIAM MONAFO (St. Louis, Missouri): It has been known for more than 25 years that extensively burned patients are hypermetabolic—appreciably more so than patients with nonthermal trauma. Since the degree of hypermetabolism is extreme, the question arises whether there may be something unique about heat-injured tissue, as opposed, for example, to tissue injury due to kinetic energy.

About 20 years ago, it was shown that thermally injured skin leaks water vapor at an abnormally high rate—up to tenfold or so more than normal. Moreover, it is known that the water vapor barrier in the skin is superficial—constituted principally by lipids in the superficial cornified layers of the epidermis, so that the cutaneous injury need not be deep in order for the barrier to be destroyed. Since the heat of vaporization of water at body temperature is nearly 0.6 calories per gram of water, it seemed likely that this additional caloric requirement was likely the principal explanation for the hypermetabolic state of the burn patient.

Subsequently, however, data from burned man apparently conflicted with this hypothesis, in that obviating evaporative water loss, for example, by covering the wounds with impermeable plastic, did not necessarily lower oxygen consumption. The situation is made more complex because core temperatures tend to be significantly elevated in burned man, a phenomenon which by itself elevates metabolic rate.

One alternative explanation that has arisen for the principal cause of burn hypermetabolism is that the hypermetabolism is primarily driven by an increase in catecholamine secretion. These are the issues addressed in the present study.

The data we have heard add weight to the concept that cutaneous evaporative water loss is indeed the most important driving force in burn hypermetabolism, since the increase in insensible water loss that attended removal of the dressings resulted in increased energy expenditure and since heat production (corrected for core temperature) was not significantly elevated above normal in these children while they were bandaged. Moreover, only when the dressings had been removed were plasma catecholamine levels significantly elevated, a finding which of course makes the mediating role of those hormones somewhat questionable.

But the design of the study was such that all patients were examined in the same sequence—that is, first with their dressings in place, and then after they had been removed. One wonders if the findings would have differed had this sequence been reversed. I therefore ask Dr. Caldwell whether he has any data collected in the reverse sequence—either from these patients or possibly from others. If he does, and if the results are similar to those in the experiments he has just reported, the data would be even more persuasive. I would also like him to say whether the increase in evaporative water loss that was observed after the dressings had been removed was statistically significant.

DR. HIRAM C. POLK, JR. (Louisville, Kentucky): I would like to speak in support of and appreciation of Dr. Caldwell's hypothesis. For some 15 years, I think he has been the clearest and most precise worker in a very, very difficult field. The work you see tonight is the culmination of a very difficult series of experiments, carried out in man under those circumstances that, I believe, are most likely to eliminate extraneous variables and present the clearest understanding of the issue.

There are three points that I think he's made well, but those of us who care for burns and have a chance to try to study this appreciate most.

The first, of course, is that the septic burn patient is a different kettle of fish, and is hypermetabolic under an entirely different set of conditions. The question he asks is: what is wrong with the nonseptic burn patient of substantial extent? He has shown two things—I think, very compelling evidence that the majority of the heat and water loss is, as hypothesized by him, Moyer, and their associates some long time ago, due to evaporative water loss. The only way that water loss is evaporated is by the core temperature of the patient exceeding that of the environment.

The second issue, which has been ignored by many people in burn care for a long time, is that the presence of occlusive dressings favorably influences hypermetabolism. This can be constructed in a number of ways, but in work we presented at the American Surgical Association we were able to show rather dramatic reductions in metabolic rate for patients when they were converted from exposed state to covered state, and that one need only be certain that the outer component of this dressing is dry to maintain most of these favorable conditions. The reverse experiments, uncovered to covered, do need to be done.

I feel that this has been an important report in a very long series of queries, and that it, as much as anything that I have heard and seen, touches most of the bases and ties the points together, as not only a valid hypothesis, but something that I think most of us can use in our burn care tomorrow.

DR. BASIL A. PRUITT, JR. (Fort San Houston, Texas): Dr. Old, Dr. Williams, Fellows and guests: I would like to reinforce Dr. Caldwell's emphasis on minimizing stress of any sort of burn patient.

His data in children are somewhat different, perhaps in degree only, than ours in adults. We find in adult patients (slide) that postburn hypermetabolism, which is burn-size related, is temperature sensitive, but not temperature dependent. That is, the increased heat production is primarily determined by metabolic factors.

(slide) Burn patients appear to have an upward alteration of central reference temperature. That is, when allowed the option of picking their temperature of comfort, it exceeds 30 C, and I think that's an important figure to remember.

(slide) Burn patients maintain increased skin and core temperatures and core-to-skin heat transfer coefficients even at temperatures between 30 and 33 C, as shown here.

Dr. Caldwell's data can be interpreted as suggesting that external heating would reduce metabolic rate, (slide) and in some of our study patients such appears to be the case; that is, with external heating, metabolic rate falls and rectal temperature rises.

(slide) But in other burn patients, the opposite occurs; that is, with central heating, metabolic rate rose, as did rectal temperature. (slide) On the average, in seven burn study patients significant elevation of rectal temperature by external heating failed to alter metabolic rate. Correction for the Q_{10} effect, as effected by Dr. Caldwell, would decrease the metabolic rate in our study patients by only 20–30%, in terms of the observed hypermetabolism.

The differences in our findings and Dr. Caldwell's prompt me to ask the following questions, in hopes of discerning the reason for these differences.

Firstly, since 28 C is below comfort temperature for burned man, was the environmental temperature actually a cold stress to the exposed patient, compared to the dressed or more insulated patient, and have you done similar studies at a higher environmental temperature?

Second, do you feel that the greater surface area per unit body mass in the child makes children more sensitive to environmental influences?

Third, since catecholamine secretion varies considerably across time, how comfortable are you with isolated measurements such as have been made? Fourth, since presumably one must supply nutrients to meet the existing metabolic needs, what purpose is served by the on-paper correction for Q_{10}?

Last, I think there is a serious methodological question about your studies as alluded to by Dr. Monafo. That is, the sequence of measurements has not been varied. Since the removal of dressings and manipulation of the patient immediately preceding exposure may impose a stress in and of itself, as reflected in the catecholamine elevation even two to four hours later, it would seem essential that some exposed patients be measured, and then subjected to wound manipulation and dressing with the same measurements made. In the absence of such data, the question which you have addressed is unanswered by this study.

Again, I emphasize how important it is that continued, careful studies in this area be made.

DR. FRED T. CALDWELL (Closing discussion): Dr. Monafo asked if we have done the reverse study, by starting the patient for 24 hours without a dressing, followed by studies after application of a dressing. The answer is no. All of our patients are treated with occlusive dressings, and they have not been studied during the period of resuscitation. We have never been able to study a burn patient, who has been treated with occlusive dressing, for more than six hours of exposure. Even in a warm environment, these patients become unmanageable due to pain and subjective cold.

Dr. Monafo also asked if the differences in the rates of heat production and evaporative heat loss between dressed and exposed states were statistically significant; the answer is yes on both counts ($p < 0.001$ for heat production; $p < 0.05$ for evaporative heat loss, $p < 0.01$ for total heat loss).

I got off lighter than I expected with Dr. Pruitt, but he asked several pertinent questions. An ambient temperature of 28 C is a cold stress for a patient with a large burn, because 28 C is thermal neutrality for nude unburned man. Clothed unburned man would be uncomfortably warm at an ambient temperature of 28 C. Dr. Pruitt asked about the greater surface area to mass ratio of children and its effect upon these data. Because of a greater surface area to mass ratio, children, much as small laboratory animals, respond more quickly than adults to a cold thermal stress. The patients in this study ranged in age from 2 to 19 years, and we did not detect an age dependence in the responses.

Dr. Pruitt asked if we were secure and satisfied with spot measurements of serum catecholamine levels, rather than measurement of 24-hour urinary metabolites of catecholamines. The half-life for serum catecholamine levels is less than 30 minutes, and we feel serial serum determinations relate far better to the clinical situation than do measurements based on 24-hour pooled urine specimens. The Q_{10} correction for heat production based on calculated average body temperature is only a pencil maneuver. However, in attempting to understand the pathophysiology of the elevated body temperature of burn patients, such a calculation may be of use.

A central question here, is increase in body temperature a primary or secondary response to thermal injury? No central metabolic set point has ever been described; however, the anterior hypothalamus contains a thermoregulatory center, which has the characteristics of having a thermoregulatory set point.

I agree with Drs. Monafo and Pruitt that patients with large burns act as if there had been a shift upward in their thermoregulatory set point.

If this is indeed true, it is of primary importance to know if this is a free-standing response or an unavoidable part of the obligatory increase in the rate of heat production, as, for example, one sees associated with physical exercise.