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Experimental Hyperthermia in Traumatic Quadriplegia

by
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INTRODUCTION

Some patients with lesions of the spinal cord may have substantial difficulty in thermoregulating under a heat stress considered mild by able-bodied persons. These patients easily develop heat exhaustion, characterized by cardiovascular irregularities, weakness and fatigue, headache, and sometimes syncope. Previous literature states that the skin of men or animals with spinal cord injury is generally anhidrotic in areas below the level of the lesion (Leithead and Lind, 1964; Randall, Wurster and Lewin, 1966; Rawson, 1963; Seckendorff and Randall, 1961). If anhidrosis is widespread, as is the case in the cervical lesions, the patient may develop hyperthermia.

Quantitative studies on spinal man reveal a significant impairment of the thermoregulatory sweat response over a wide area of the body. Guttmann, Silver and Wyndham (1958) observed the behavior of the core temperatures of spinal man in the warm air of open wards. Patients with high cervical lesions were largely anhidrotic over their body surface and had difficulty in maintaining normal body temperature. Nevertheless, Randall, Wurster and Lewin(1966) concluded that the isolated spinal cord is still capable of mediating a sweat reflex as did Cooper, Ferres and Guttmann (1951).

We surmised that quadriplegics might become hyperthermic when exposed to high ambient temperatures or to exercise. Therefore, we studied quadriplegic subjects under a controlled heat stress and measured their thermoregulatory responses, thereby further characterizing quantitatively the quadriplegic disability.

MATERIALS AND METHODS

SUBJECTS: Six men, each having chronic spinal cord injury in the cervical region (C8 to C3), participated in these experiments. Descriptions of their disability, age, and medications are given in Table 1. Nine control experiments were conducted on three able-bodied men under conditions identical to those in the quadriplegic experiments. Table 2 gives the characteristics of all the subjects. Each subject was tested every time at approximately the same time of the day.

CONDITIONS: The subjects were submitted to total body heat exposure in an environmental chamber. Base line readings were taken at room temperature, prior to entering the hot chamber. Room conditions were T_a 25°C and 50% rh, while those in the hot chamber were T_a 38°C and 9% rh. Following base line readings for one hour the subjects were transferred into the environmental chamber for a maximum of $2\frac{1}{2}$ hr. The subject sat inactive throughout the experimental period.

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TABLE 1. Characteristics of the quadriplegic subjects

Subject	Sex	Age	Disability	Medication	Years since onset of disability
F.F.	M	25	C5-8 with C2 sensation on right side	none	9
E.S.	M	19	C6 fusion, laminectomy	none	2
J.W.	M	19	C6 laminectomy	none	3
W.D.	M	33	C5-6 fusion, laminectomy	tetracycline (occasional)	13
C.L.	M	21	C6-7 fusion, laminectomy	none	5
E.H.	M	22	C6-7 laminectomy	valium (4 mg/day)	4

TABLE 2. Physical characteristics of all subjects*

Subject	Age (yr)	Height (cm)	Weight (kg)	Surface area (m^2)
		Quadriplegic men		
W.D.	33	178	52.2	1.68
C.L.	21	175	58.3	1.72
J.W.	19	185	57.0	1.78
E.S.	19	178	62.8	1.79
F.F.	25	185	85.7	2.10
E.H.	22	173	51.4	1.60
Mean	23	179	61.2	1.78
		Able-bodied men		
H.E.	19	183	83.3	2.10
R.B.	20	185	73.9	1.96
B.R.	20	181	85.0	2.08
Mean	20	183	80.7	2.05

*) All were men aged over 18 years.

The experiments were terminated when signs or symptoms of heat illness appeared, when the oral temperature reached 38.5°C or when the subject himself decided to stop.

PARAMETERS: The following measurements were made.

(a) Oral temperature (T_{or}) was measured by means of a multipoint Honeywell galvanometer, recording at one minute intervals.
(b) Heart rate and respiration rate were monitored continuously by telemetry (Telemedics, Southampton, Pa.), recorded with an Offner Dynograph.
(c) Blood pressure was measured before entering the chamber and just prior to termination of the experiment.
(d) Local sweat rate was measured at selected sites, with unventilated sweat capsules (Schwartz, Thaysen and Dole, 1953). To collect the sweat, two circular pieces of filter paper (area = 14.3 cm^2 each) were held firmly to the skin by aluminium sweat capsules and an elastic strap. Sweat was collected at six locations for two 30-min collection periods. These sites included symmetrical sides of the back of the neck, the volar surface of the forearm, and the anterior surface of the thigh, just above the knee. At the end of each collection period, the filter papers were placed in Scotch-pak aluminized polyethylene bags (Johnson, Johnson and Sargent, 1969) and immediately reweighed.
(e) Total body weight loss was calculated as the difference in weight before and after the heat exposure.
(f) The volume and composition of the subjects' expired air were measured at 30-min intervals throughout the experiment. The expired gas was collected by means of an open circuit technique. A sample of each 30-min collection was analyzed for oxygen with a Beckman O_2-meter (model C_2) and for carbon dioxide with a Godart CO_2 meter (Type 44A-2). The two machines were arranged in series. See Consolazio, Johnson and Pecora (1963) for the specific calculations.

STATISTICAL ANALYSIS: The responses of each group of subjects, after heat exposure, were compared with their own resting levels measured before the heat stress. The responses of the two groups were then contrasted both before and after the heat exposure. The data were subjected to a t-test (Huntsberger, 1967) to determine the probabilities of differences between means, and 0.05 or less was chosen as significant.

RESULTS

The three most interesting findings were the controlled production of hyperthermia among the quadriplegics, the demonstration that there was a defect in evaporative heat loss, and the development of true panting during hyperthermia.

HYPERTHERMIA: Nineteen experiments were performed on 6 quadriplegic men. In all cases, hyperthermia developed before the conclusion of the 150-min heat stress. The mean oral temperature rose from a base line of 36.8° to 38.7°C after 120 min of exposure ($n = 18$, $p < 0.05$). In those experiments where the subject endured through the full 150 min, T_{or} rose to 38.8°C after 150 min ($n = 9$, $p < 0.005$). The quadriplegics developed panting and distress and usually elected to end the heat exposure after 120 min rather than the planned 150 min.

Nine control experiments were done on 3 able-bodied volunteers. The same protocol was followed as for the quadriplegics. These control subjects were comfortable for the full 150 min, with no significant changes in physiological functions.

Striking differences in responses of the two groups are seen in a plot of the oral temperature against time (Fig. 1). The quadriplegics developed hyperthermia soon after entering the environmental chamber, while the able-bodied men maintained a normal body temperature throughout the experiment ($p < 0.005$ for the 120-min period).

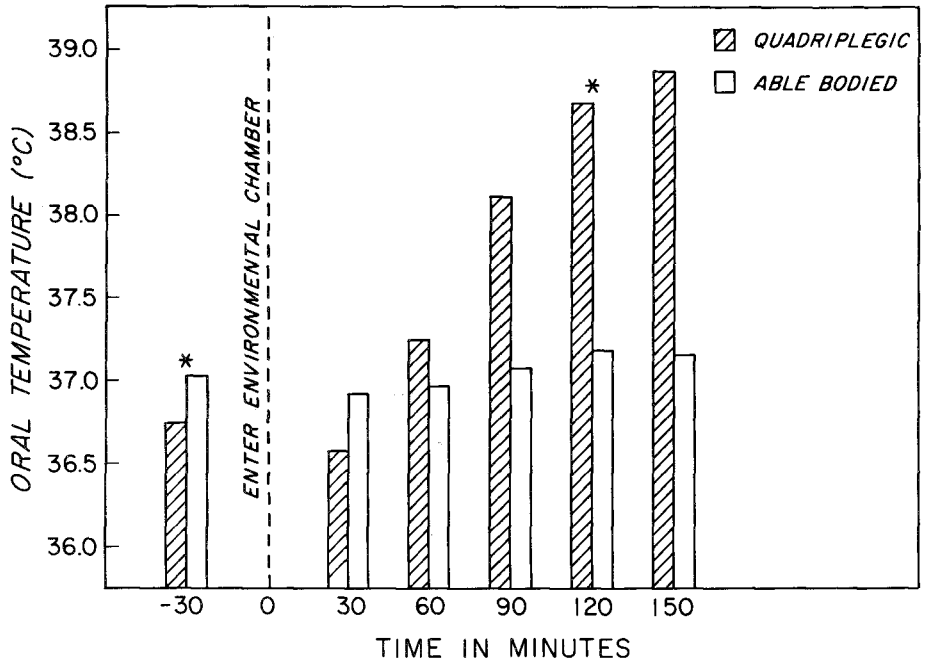

Fig. 1. Oral temperature versus time for quadriplegics and able-bodied controls. Asterisk denotes $p = 0.05$ or less at 120 min.

EVAPORATIVE WATER LOSS: The total loss of weight was three times as great in the able-bodied men as in the quadriplegics (Table 3).

The only contributions to this weight loss were metabolic, i.e. the difference in weight between O_2 consumed and CO_2 produced, pulmonary water loss and dermal water loss. Urine and faeces were retained in sanitary bags on the wheelchair, and did not contribute to the loss of weight. Metabolic weight loss was small and not important. Pulmonary ventilation became greater in the quadriplegics (Fig. 2) and therefore, the pulmonary water loss was greater in the quadriplegic men, even though they were smaller than the able-bodied men. The percentage of weight loss due to pulmonary evaporation was much greater in the quadriplegics. In contrast, the dermal loss was four times as large in the able-bodied men as in the quadriplegic men. Presumably in the quadriplegics it was mainly insensible water loss, and in the able-bodied subjects mainly eccrine sweat. This supposition was confirmed by local measurements. The able-bodied controls averaged 44 mg/30 min-capsule area for 108 measurements. The quadriplegics were anhidrotic.

The complete equation for thermal balance is:

$$M = E \pm R \pm C \pm K \pm W \pm S \qquad (1)$$

where M is metabolic heat, always positive; E is evaporative loss, always positive; R is radiation,+ for net loss; C is convection,+ for net loss; K is con-

TABLE 3. Mean values for weight loss contrasting quadriplegic subjects with able-bodied controls

	Quadriplegic[a]		Able-bodied[b]	
	Weight loss (g)	Fraction of weight loss (%)	Weight loss (g)	Fraction of weight loss (%)
Total body	212	100	648	100
Metabolic[c]	13	6	5	1
Pulmonary[d]	56	27	42	6
Dermal[e]	143**	67	601	93

a) Eighteen experiments with six men.
b) Nine experiments with three men.
c) Calculated as the difference in weight between CO_2 produced and O_2 consumed.
d) Calculated as the difference in weight H_2O expired and H_2O inspired, calculated from volume and absolute humidity (Lange, 1961).
e) Calculated as the difference between total body loss and the sum of metabolic and pulmonary loss. Among the quadriplegics the skin was dry to the touch, and little or no active sweating was detectable by local collection.

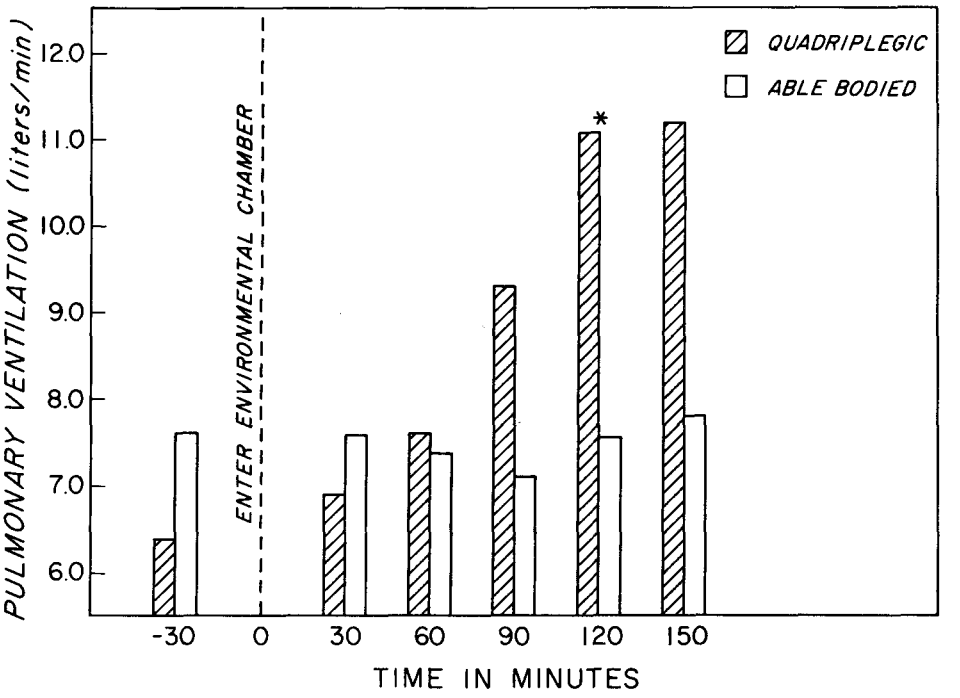

Fig. 2. Pulmonary ventilation versus time for quadriplegics and able-bodied controls. Asterisk denotes p = 0.05 or less at 120 min.

duction, + for net loss; W is work performed, + for work against external force; and S is heat stored, + for gain. In the present system, R, C and K were effectively zero, because the wall, air and wheelchair temperatures were all very near to that of the skin. W was zero because the subjects were sitting quietly. For this set of circumstances, then, Equation 1 transforms to:

$$S = M - E \quad (2)$$

S was measured by the change in body temperature, M was calculated from the O_2 consumption, and E was calculated from the insensible water loss. In the able-bodied subjects, S was zero in 2 hr, and thermal balance was achieved. In the quadriplegics, S was positive and hyperthermia resulted. M did increase by about 20% in the quadriplegics, but E did not increase proportionately (Fig. 3 and Table 3). The cause of the hyperthermia, therefore, was a defect in the evaporative heat loss.

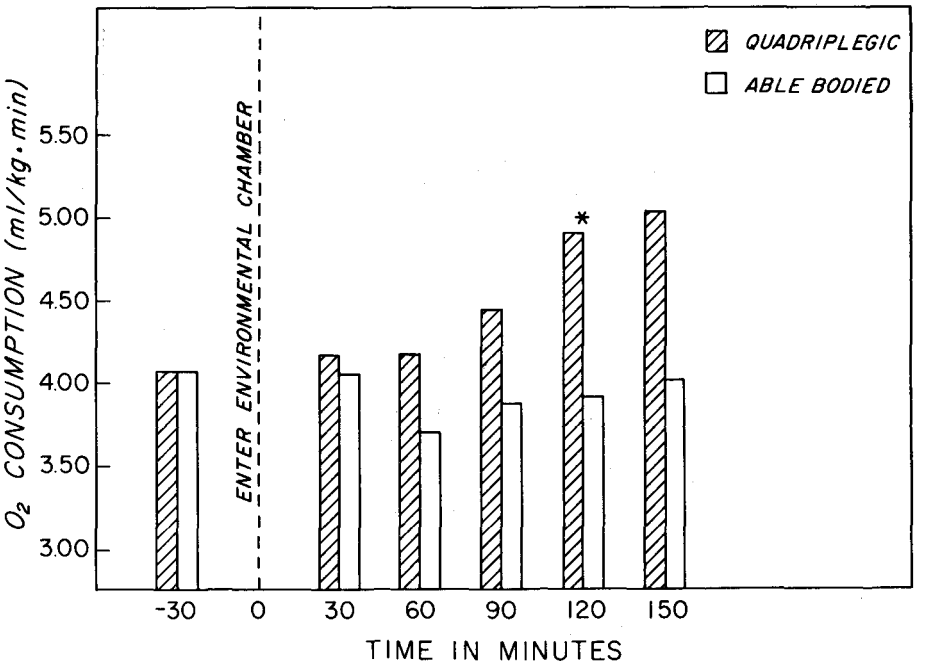

Fig. 3. O_2 consumption versus time for quadriplegics and able-bodied controls. Asterisk denotes p = 0.05 or less at 120 min.

PANTING: Panting may be defined as an increase in the pulmonary minute volume caused by an increase in rate with little or no change in tidal volume. By these criteria, panting occurred in the quadriplegics but not in the able-bodied controls.

The pulmonary ventilation increased linearly with the body temperature (Fig. 4).

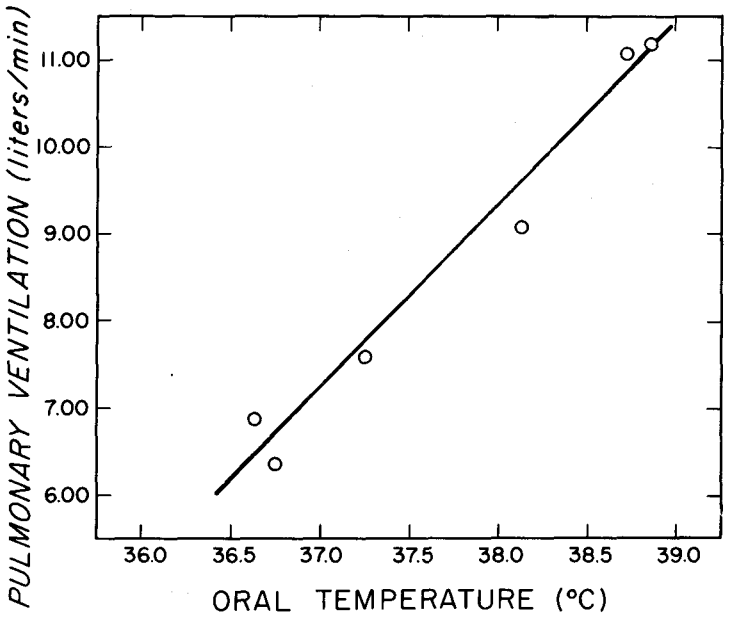

Fig. 4. Pulmonary ventilation versus oral temperature for quadriplegics

DISCUSSION

The neurological disabilities of the traumatic paraplegic and quadriplegic offer opportunities for research into the control of heat balance. To take one example, the occurrence of anhidrosis suggests a lack of thermal recognition, based on peripheral interruption of nervous connections. The occurrence of panting, however, clearly supports the probability of central recognition of thermal stimuli and a defect in the response, not the sensorium. The panting response acts like a proportional response to an error signal.

The O_2 consumption of the quadriplegics,after a break-point, rises linearly with body temperature (Fig. 5). We do not know the cause of this proportional increase but insofar as thermal balance is concerned, we interpret the curve to mean that below a critical O_2 consumption, the heat can be dissipated, but above the critical point, heat storage becomes positive in direct relation to O_2 consumption. Exposure to the cold causes a rise in O_2 consumption in the absence of peripheral receptors (Downey, Darling and Chiodi, 1967; Johnson, Smith and Spalding, 1963; Johnson and Spalding, 1966). Therefore, quadriplegics do have some central recognition of thermal stimuli and can alter the energy metabolism.

In man evaporative loss from the lung is usually regarded as minor and unregulated in comparison with dermal evaporative loss (Belding and Hertig, 1962; Gagge, 1964; Hardy, 1961; Thauer, 1961). Yet in some warm-blooded vertebrates pulmonary evaporative loss is a main avenue of heat control. True panting is not generally considered as one of man's regulated functions. We have demonstrated it now among quadriplegics, clearly as an atavistic, even if ineffective, response to thermal stress. In able-bodied men the evaporative pulmonary loss can increase fifteen-fold or more from rest to maximal exercise, but even so the eccrine sweat glands far exceed the lungs as a site of evaporative heat loss. In the quadriplegics, the lungs cannot substitute for the sweat glands and hyperthermia easily results.

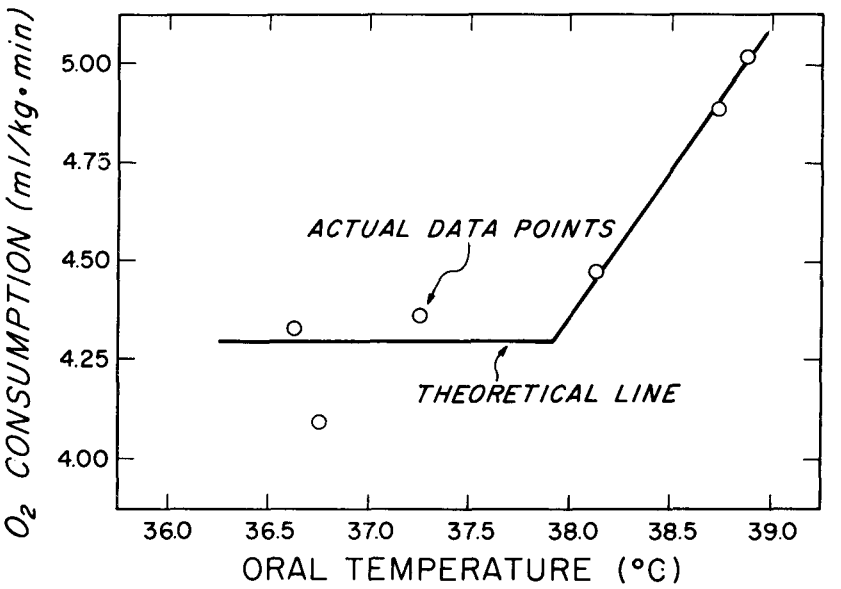

Fig. 5. O_2 consumption versus oral temperature for quadriplegics. The "theoretical line" shows a break where compensation is no longer possible, and hyperthermia ensues as a result of an increase in stored metabolic heat. The data points are means for quadriplegic subjects.

Most current models of thermal regulation in man have adopted the concept of Hardy and his group (Hammel et al., 1963; Hardy, 1961) that regulation is proportional to deviations from a set-point anatomically located in the hypothalamus. Sometimes the set-point varies (Brengelmann and Patton, 1966) in different physiological states such as cold exposure or fever. The quadriplegic lacks the peripheral connections for heat regulation. This phenomenon has been observed or postulated both experimentally (Pembrey, 1897; Sherrington, 1924) and clinically (Cooper, Ferres and Guttmann, 1951; Guttmann, Silver and Wyndham, 1958; Rawson, 1963; Rawson and Hardy, 1967). Not only does the quadriplegic lose thermal regulation by dermal evaporation, but also by loss of vasomotor control.

Some observers have detected reflex sweating below the lesion (Pollock et al., 1951; Randall, Wurster and Lewin, 1966). Such residual reflexes cannot be effective in thermoregulation, because the anhidrosis of quadriplegics never recovers spontaneously in our experience or that of others (Leithead and Lind, 1964). Nevertheless, it is true that sweat glands below the lesion can be "trained" to activity by daily intradermal injections of cholinergic drugs (Johnson and Johnson, 1970). The possibility exists then that peripheral stimulation still may exist potentially in quadriplegics.

Our results have practical as well as theoretical implications. Three of our subjects (F.F., E.S. and J.W.) measured their own temperatures hourly during a mild spring day in May. Ordinary activity, such as wheeling to class raised the oral temperature as high as 38°C. Instruction about how to avoid or take care of hyperthermia should be part of the training of these people, just as they are taught about decubitus ulcers and urinary tract infections.

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