Relationship of Increased Oxygen Consumption to Catecholamine Excretion in Thermal Burns

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THE SERIOUSLY burned patient is known to increase oxygen consumption for extended periods of up to three months following the burn injury. In the search for an explanation of this occurrence Morgan *et al.*[12] identified a greatly increased loss of water vapor in the postburn period and suggested that the heat energy required to vaporize and maintain this large insensible water loss is one reason that more oxygen is utilized after a burn. In their initial description of this phenomenon of hypermetabolism in burned patients Cope *et al.*[4] found no related increase in thyroid hormone secretion to account for this increase in oxygen consumption.

We have been puzzled by the normal thyroid function in burn patients and have been searching for another biochemical stimulus of oxidative metabolism that postburn patients could use in meeting energy demands. In this connection the simultaneous reports of Birke *et al.*[2] and Goodall *et al.*[7] in which greatly increased adrenalin and noradrenalin excretion were described in seriously burned patients were of great interest to us. Observations of Hörstmann,[9] Bernstein *et al.*[1] and Moore and Underwood[11] made it clear that catecholamines will stimulate increase in oxygen consumption and this has appealed to us as a possible adaptive mechanism of importance in furnishing energy to the burned patient. This study demonstrates that increases in oxygen consumption and catecholamine excretion occur simultaneously in seriously burned patients and further demonstrates a significant correlation between the magnitude of oxygen consumption increase and the degree to which catecholamine excretion is elevated.

Methods

Oxygen consumption was repeatedly determined with a Benedict-Roth spirometer in 30 adult patients with thermal burns of greater than 40% of estimated body area. Six of these patients had elevated metabolic rates which persisted beyond the first two postburn weeks. These six patients were studied in detail with weekly determinations of free adrenalin and noradrenalin excretion and simultaneous measurement of oxygen consumption. In all instances at least two metabolic rate determinations were made during each 24-hour urine collection to obtain a value of maximum reliability. Urinary adrenalin and noradrenalin were measured by the well-standardized fluorometric technic of von Euler and Lishajko[13] which takes advantage of the oxidation of these amines to highly fluorogenic trihydroxy-indole forms. None of the six patients was hyperthyroid and none was persistently febrile through the time of

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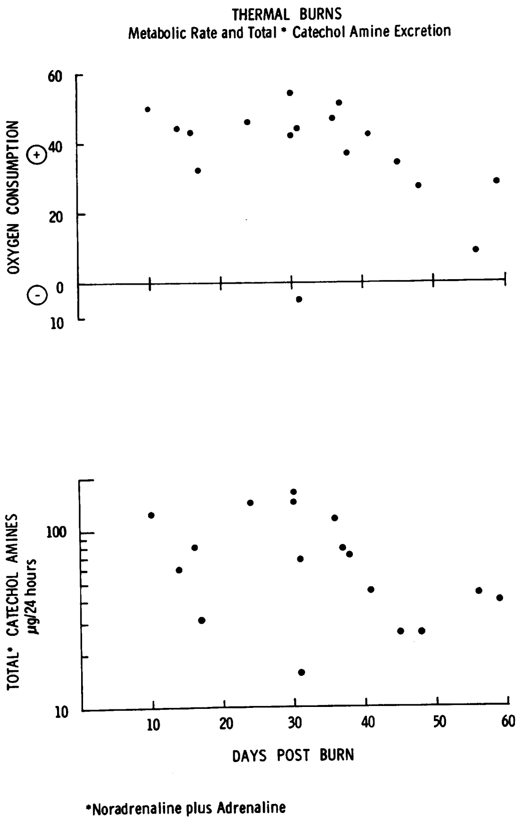

FIG. 1. Metabolic rate values, expressed as percent above or below the predicted normal, and total free excretion of adrenaline plus noradrenaline are shown in relation to their day of occurrence in the postburn period.

study. All patients were studied weekly until both oxygen consumption and catecholamine excretion returned to normal.

To evaluate results critically we individually plotted the total free excretion of the two catecholamines (Fig. 2), noradrenalin (Fig. 3) and adrenalin (Fig. 4) against corresponding abnormal metabolic rates. A logarithmic scale was used for catecholamines to demonstrate whether or not the values approach a conventional dose response relationship. Mean curves and their regression values on the ordinates represent an ideal fit to the data obtained by the method of least squares as outlined by Mainland.[10] Linear correlation co-efficients were determined by methods derived from Fisher's tables.[6]

Results

In the six patients studied in detail, both oxygen consumption and elevated catecholamine excretion reverted to normal by the 50th postburn day. As seen in Figure 1, the decline in catecholamine excretion appears to precede the fall in metabolic rate by approximately one week, but there is insufficient data to critically examine this point. We consider a metabolic rate of greater than $\pm 20\%$ to be abnormal in these circumstances since it is generally impossible to study burned patients in ideally basal conditions. Normal free catecholamine excretion with the analytical techniques used have been defined by von Euler and Lishajko as 15.7 ± 2.2 μg./day for noradrenalin and 5.6 ± 1.3 μg./day for adrenalin.

Figure 2 shows the total of these two catecholamines, noradrenalin plus adrenalin, in relation to all oxygen consumption values in excess of $+20\%$. The correlation is significant as shown, $p < 0.01$, and re-

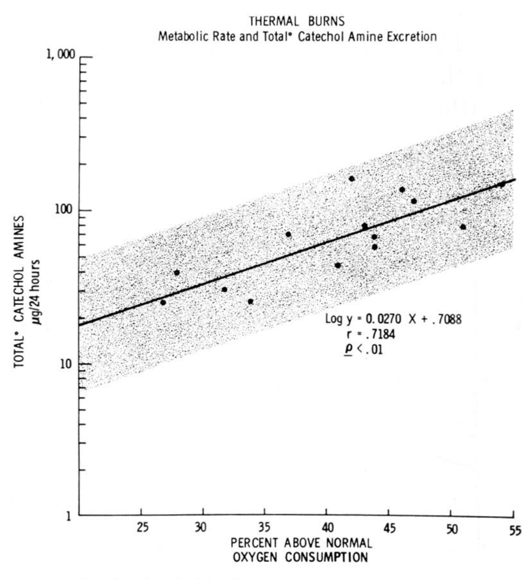

FIG. 2. Metabolic rate is plotted against total free excretion of adrenaline plus noradrenaline on the vertical logarithmic scale. The stippled area represents two standard deviations on each side of the ideal mean curve.

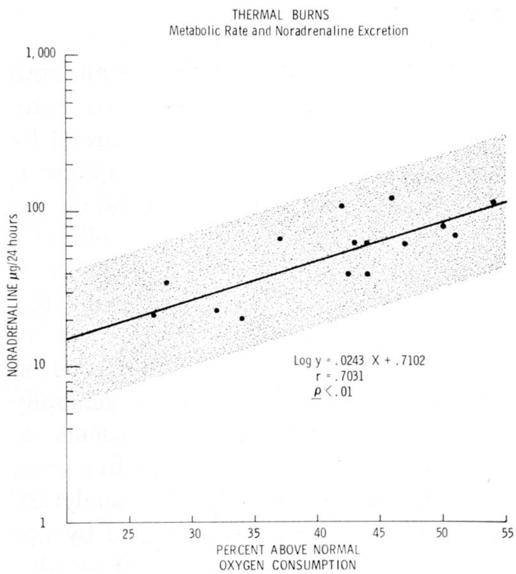

FIG. 3. Metabolic rate and free 24-hour noradrenaline excretion are plotted with two standard deviations on each side of the ideal mean curve.

gression of the ideal curve to a metabolic rate of +20% reveals a figure for total catecholamine excretion well within the normal daily range.

In Figure 3 the values for free noradrenalin excretion are treated in the same way. The correlation is not quite as strong as with the total catecholamines, but is, nevertheless, significant at the $p < 0.01$ level and the regression value for noradrenalin excretion is normal at a metabolic rate of +20%.

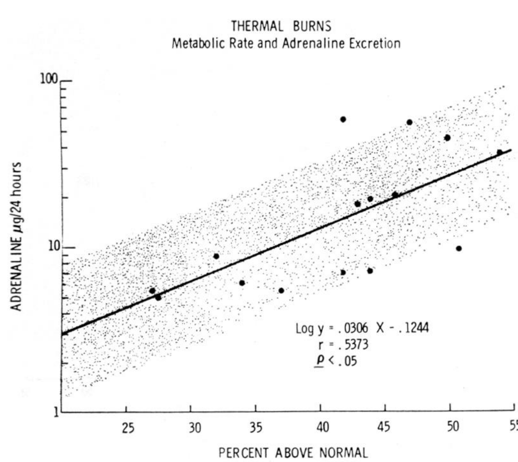

FIG. 4. Free adrenaline excretion and corresponding metabolic rate values are shown with two standard deviations on each side of the ideal curve.

Greater variability of adrenalin excretion in relation to the observed metabolic rates is apparent in Figure 4. Two values are seen to fall beyond the ±2 standard deviations of the mean represented by the stippled area. The relationship between metabolic rates and excretion of adrenalin is, however, of probable significance, $p < 0.05$.

Discussion

There can be no doubt that energy requirements of the postburn patient are great. We previously alluded to the studies of Morgan *et al.*[12] defining an increased production of water vapor as one factor contributing to added energy requirements and this has been amplified by later studies of Caldwell *et al.*[3] The obvious mechanism to increase energy available through oxidative metabolism might logically be thyroid hormones. Convincing evidence that thyroid function is normal in hypermetabolic burn patients was set forward by Cope *et al.*[4].

There is evidence that administration of exogenous catecholamines increases oxygen consumption,[1, 9, 11] and there is no reason to suppose that endogenously liberated catecholamines are any less effective in this respect. For these reasons it is probable that increased catecholamine secretion is responsible for the elevated metabolic rate seen in burned patients. At least two major biologic sources of energy, glycogen and fat, are broken down under enzymatic influences sensitive to adrenalin stimulation. Hornbrook and Brody[8] described the activity of a phosphorylase in myocardium and striated muscle which is specifically activated by adrenalin, and Dole[5] described lipase activity in man which is highly sensitive to adrenalin stimulation with the resulting liberation of free fatty acids into the circulation.

Summary

Co-existence of increased metabolic rate and elevated free excretion of adrenalin and noradrenalin is described in seriously burned patients. There is a significant correlation between the degree of metabolic rate increase and corresponding increases in free excretion of these catecholamines.

These findings are discussed in relationship to significance in providing burned patients with increased energy from oxidatively available stores in fat and muscle. Some reasons for this increased energy requirement of the burned patient are discussed.

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