Elevation of Peripheral Blood Ammonia Following Muscular Exercise. (24103)

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Hyperpnea observed during and immediately following muscular exercise has been ascribed to changes in blood pH, PCO_2, anoxia, and reflexes from exercising muscles or great veins. These alterations do not appear to account completely for the intensity of hyperpnea(1). It has been suggested, therefore, that there is still an unrecognized respiratory stimulant contributing to increase in ventilation during and following muscular exercise. The possible role of ammonia in this respect is worthy of consideration. Respiratory alkalosis in patients with elevated blood ammonia due to hepatic coma has been well documented. Infusion of neutral ammonium salts into normal dogs also produces respiratory alkalosis(2). It is known, too, that the ammonia content of venous blood draining an exercising forearm is elevated(3). Peripheral systemic blood ammonia has not been measured following voluntary muscular exercise. Studies were carried out in human and animal subjects to 1) determine if there is significant elevation of peripheral blood ammonia following voluntary muscular exercise or following convulsions induced by electro-shock or metrazol, and 2) correlate changes in blood ammonia with changes in ventilation following muscular exercise.

Methods. Alterations in blood ammonia in various types of muscular exercise have been studied as follows: 1) muscular exercise induced by electroshock therapy in humans or by metrazol in dogs, and 2) voluntary muscular exercise in normal human males (running). In both groups blood ammonia, pH, and plasma total CO_2 content were measured during a control period and at suitable intervals following exercise or convulsions as indicated in Fig. 1 through 4. Blood ammonia was analyzed by the method described by Bessman and Bessman(4). Minute respiratory volume was measured only on normal human subjects prior to, and following, voluntary muscular exercise. These measurements were carried out using a Tissot Gasometer. Studies of patients subjected to electroshock therapy were carried out under 2 conditions: 1) a group of 9 psychiatric patients who received only atropine as premedication and had violent generalized muscular contractions for approximately one minute (Group 1); and 2) 5 patients who received anectine, surital and atropine prior to electroshock therapy, thereby largely preventing motor aspects of the convulsions (Group 2). In 3 anesthetized dogs convulsions were induced by administration of 40-160 cc of metrazol in 1-3 cc increments at rate sufficient to produce severe muscular movements. Duration of convulsions by this method was 5, 25, and 30 minutes. Arterial blood was used for chemical analysis.

Results. Alterations in patients subjected to electroshock therapy: The data in Fig. 1 illustrate changes in blood ammonia, pH, and plasma total CO_2 in 9 psychiatric patients given electroshock therapy accompanied by marked convulsions (Group 1).† In 6 patients there was an elevation of blood ammonia, and decrease in pH and total CO_2 immediately following convulsions. In 2 of 3 other patients, blood drawn after 20 minutes showed ammonia levels which were similar to control values. Data shown in Fig. 2 illustrate minimal alterations in 5 patients who, due to premedication, did not have muscular convulsions following electroshock therapy (Group 2). In this group only one patient displayed a slight elevation of blood ammonia, and he had a

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† The calculated PCO_2 values in these patients before shock were 4-5 minutes Hg higher than normal. We have no explanation for this.

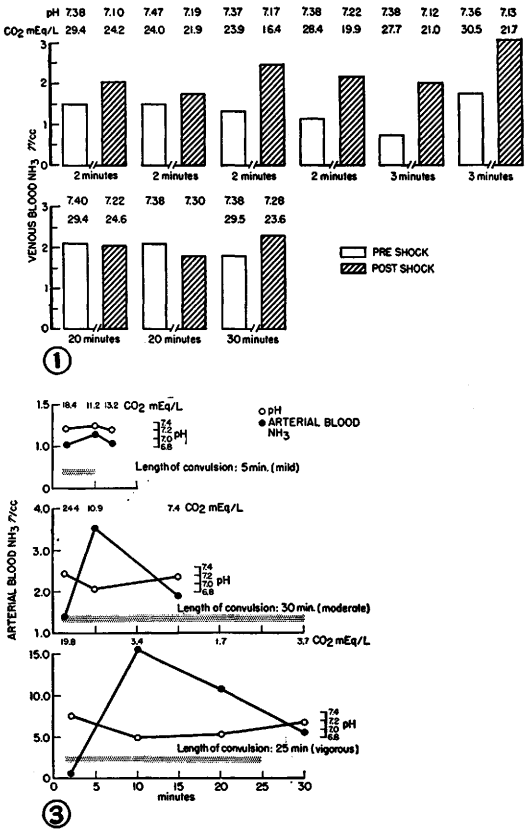

FIG. 1. Blood ammonia and acid-base alterations in 9 patients subjected to electroshock therapy accompanied by active convulsions.

FIG. 2. Blood ammonia and acid-base alterations in 5 patients subjected to electroshock in whom active convulsions were prevented by premedication.

FIG. 3. Blood ammonia and acid-base alterations in 3 dogs following metrazol convulsions.

FIG. 4. Blood ammonia and respiratory minute vol after severe exercise for 5 min. (human subjects).

small convulsion despite premedication.

Alterations in dogs given metrazol. There was a marked decrease in blood pH and plasma total CO_2 in dogs with convulsions following metrazol administration (Fig. 3). The rise in peripheral blood ammonia was also striking. Changes in blood ammonia, pH, and plasma CO_2 were greater than were measured in human subjects given electroshock therapy.

Changes in blood ammonia following muscular exercise: The data in Fig. 4 show the increase in blood ammonia at intervals up to 20 minutes following 5 minutes of voluntary strenuous muscular exercise in normal adult males. In the 3 subjects studied, the maximal elevation of blood ammonia was not reached until 2-6 minutes after the exercise was completed. The maximal elevation of blood ammonia could not be closely correlated with the maximal increase in minute volume. There was, however, a significant elevation of blood ammonia during the hyperpneic period following exercise. The blood pH and plasma CO_2 also decreased following muscular exercise.

Discussion. A combined metabolic and respiratory acidosis was observed following both artificially produced convulsions and voluntary exercise. These changes were, to some extent, a measure of magnitude of muscular activity. Of most interest to us were the small, but consistent, elevations of blood ammonia that occurred both after voluntary exercise and convulsive states.

The experimental production of metabolic or respiratory acidosis has been shown to cause some increase in blood ammonia in normal and Eck fistula dogs(5). This is of importance because most of the rises in blood ammonia were associated with decrease in blood pH. There were 2 observations, however, that suggested these changes in blood ammonia with exercise were of additional significance. Dogs subjected to mild voluntary exercise demonstrated elevation of blood ammonia in the post-exercise period, despite lack of significant change in blood pH. Also, a decrease in pH by acid infusion was associated with much smaller rise in blood ammonia than a comparable change in pH occurring after experimentally produced convulsions(5).

The source of the increase in blood ammonia would seem to be from within the muscles themselves as a result of deamination. Earlier work with isolated muscle suggests that ammonia formation is more prominent following the period of muscle fatigue than during the active period of contraction(6), and this is supported by the observed changes in blood ammonia in this study.

Although the respiratory stimulant, ammonia, was elevated following muscular exercise or active convulsive states, the actual significance of this observation is not entirely clear. The peak of increase in ventilation was immediate in the post-exercise period, but maximal elevation of blood ammonia did not occur until approximately 4 minutes post-exercise. Ammonia elevation which did occur, persisted to some extent after ventilation had returned to control values. The increase in cardiac output and oxygen consumption with muscle exercise also continues for a longer period than the hyperpnea. The possibility that ammonia plays some role in normal respiratory response to exercise is suggested by the consistent observation of increased blood ammonia following various forms of exercise studied.

Summary. 1. Peripheral blood ammonia concentrations were elevated following convulsions due to electroshock therapy in patients, convulsions in dogs due to metrazol, and active voluntary exercise in human subjects. 2. The possibility that increase in circulating blood ammonia may be a factor in hyperpnea of muscular exercise is discussed.

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Electromagnetic Blood Flow Meter Yielding a Base Line Without Interruption of Flow.* (24104)

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The latest modification of the electromagnetic flowmeter(1) constitutes an improvement over previous forms(2,3,4) in that it permits recording of blood flow in essentially freely moving conscious animals. But 2 problems remained to be solved to make it an instrument of unrestricted usefulness in physio-

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