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Effects of Cardiovascular Surgery on Blood Concentrations of Taurine and Amino Acids[1] (41204)

J. B. LOMBARDINI[2] AND DONALD L. BRICKER

Departments of Pharmacology and Therapeutics and Surgery, Texas Tech University Health Sciences Center, Lubbock, Texas 79430

Abstract. Concentrations of taurine and other amino acids were measured in whole blood and plasma of patients who were subjected to either cardiac surgery which involved known cardiac trauma or noncardiac vascular surgery in which cardiac trauma was not expected. In all surgical procedures within 24 hr taurine levels in whole blood increased by 50 to 80% above control values. The concentration of taurine in plasma did not increase postsurgery thus indicating that a cellular component(s) of the blood was sequestering taurine. Fluctuations were also noted in the blood levels of some of the other amino acids but the changes were either not as pronounced as were the taurine elevations or were decreases in concentration. The results indicate that fluctuations in blood taurine levels do not constitute reliable indices to quantitate myocardial injury in the postoperative patient.

Taurine, a nonessential amino acid, is known to be concentrated in cardiac tissue (1). Although the precise metabolic effects of trauma in the myocardium have not been defined, previous studies in our laboratory demonstrated that taurine was released in significant quantities from the stressed or injured myocardium in animal models (2–4). It was also documented that, in the human, blood taurine levels increased after acute myocardial infarction (5). Because of these findings, it appeared that the monitoring of taurine levels could possibly assume clinical importance in quantitating degrees of myocardial injury in much the same manner as serum glutamic–oxaloacetic transaminase, lactate dehydrogenase, and creatinine phosphokinase MB fraction.

In order to investigate this hypothesis, the current study was designed to evaluate changes in taurine and other amino acid concentrations before and after surgery in patients undergoing elective surgical procedures involving the cardiovascular system, and compare these changes with a known clinically useful indicator of myocardial damage, creatinine phosphokinase MB fraction. The surgical procedures included coronary artery bypass, cardiac valve replacement, abdominal aortic aneurysmectomy, and aortofemoral bypass.

Methods. Patients admitted to St. Mary of the Plains Hospital for cardiac operation were subdivided into the following groups: Group I, consisted of patients who underwent coronary artery bypass; Group II, mitral or aortic valve replacement; Group III, resection of abdominal aortic aneurysm; and Group IV, aortofemoral bypass procedures.

Patient blood samples were obtained from the antecubital vein upon admission to the hospital (ADM) at least 2 days prior to surgery. On the day of surgery premedication included morphine and anticholinergic agents. Following induction of general endotracheal anesthesia, a left percutaneous radial artery catheter was placed and a right percutaneous subclavian venotomy was performed for continuous monitoring of arterial and venous blood pressures. At this stage in the operative procedure both a venous and arterial blood sample were drawn and designated as "presurgery (PRE)." Immediately after the surgical procedure a series of blood samples were drawn from the radial artery or subclavian vein and designated 0, 12, 24, and 48 hr postsurgery.

Blood samples were subdivided into two

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[2] To whom reprint requests should be addressed.

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portions. One part was deproteinized with an equal volume of 5% perchloric acid and centrifuged for 15 min at 10,000*g*. The supernatant solution was stored frozen until analysis could be performed. Platelet-free plasma was obtained from the second portion of the blood by centrifuging for 15 min at 10,000*g*. The plasma was then deproteinized and centrifuged under the same conditions employed for the blood samples.

Taurine content was determined in the blood or plasma samples on an amino acid analyzer (Beckman Model 121) utilizing W-1 resin (Beckman Co.) and sodium citrate buffer (0.2 *N*, pH 2.4).

Concentrations of individual amino acids in blood were determined by utilizing PA-28 resin (for acid and neutral amino acids) and PA-35 resin (for basic amino acids) and sodium citrate buffers as outlined in the Beckman Manual for the Model 121 amino acid analyzer. Glutamine and asparagine eluted as a single peak under the conditions employed.

Creatinine phosphokinase isoenzyme (CPK-MB) concentrations were measured electrophoretically by the clinical laboratory staff of St. Mary of the Plains Hospital (method of Helena Laboratories, Beaumont, Tex.).

Kruskal–Wallis and/or pairwise Wilcoxon 2-sample tests for nonparametric data were utilized for determining statistical differences between groups of data.

Amino acids data are reported in μmole · liter^{-1} and are expressed as means ± SEM.

Results. In 15 patients undergoing coronary artery bypass procedures (Group I), the concentration of taurine in blood increased significantly during the operative procedure (Fig. 1). Statistical differences were computed using the presurgery taurine value as a reference point. Taurine concentrations reached a maximum at 24 hr and then started to decrease at 48 hr postsurgery. Plasma concentrations of taurine (Fig. 1) demonstrated no fluctuations during the postoperative recovery period.

Comparisons between the taurine contents of blood and plasma samples obtained from patients upon admittance (ADM) to the hospital and immediately prior (PRE) to surgery (but after induction of anesthesia)

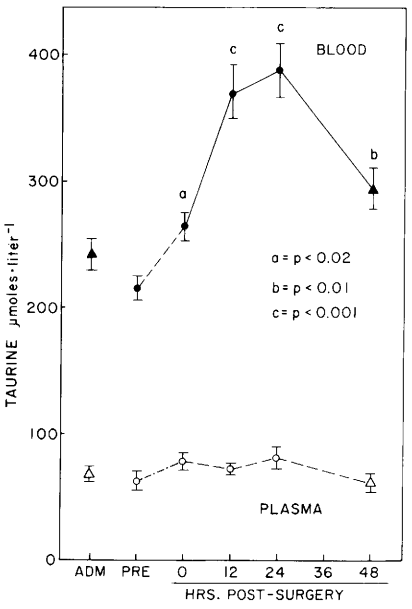

FIG. 1. Pre- and postoperative taurine concentrations in blood and plasma from 15 patients undergoing coronary artery bypass surgery. Arterial blood is designated by the symbols ○ or ●; venous blood is designated by △ or ▲. Presurgery taurine values (PRE) were used as the reference point for comparisons to the postsurgery values.

are shown in Fig. 2. No differences in taurine content were noted between presurgical venous and arterial blood or plasma samples. Concentrations of taurine in venous blood and plasma obtained upon admission of the patient to the hospital were significantly greater ($^{a}P < 0.005$; $^{b}P < 0.05$) than the levels found in venous samples taken immediately prior to surgery. These blood samples were drawn approximately 2 days apart.

Seventy patients receiving coronary grafts (Group I) were subdivided into four subgroups; 14 patients received one graft; 20 patients received two grafts; 31 patients received three grafts; and 5 patients received four grafts (Fig. 3). In addition, blood from 10 patients undergoing mitral or aortic valve replacements (Group II) were also analyzed for taurine content. The general pattern of an increase in blood concentrations of taurine after surgery was similar to that reported in Fig. 1. Note that the taurine values of postsurgery *arterial* blood

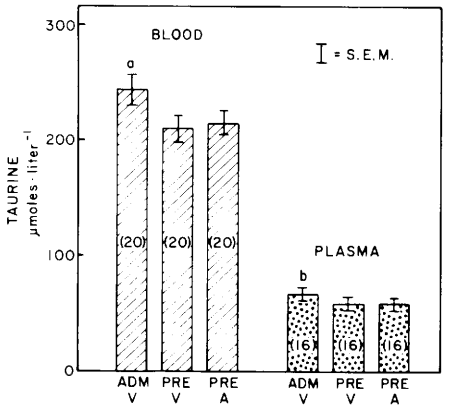

FIG. 2. Comparisons between the concentrations of taurine in venous (V) and arterial (A) blood and plasma obtained from patients undergoing coronary artery bypass surgery. ($^aP < 0.005$; $^bP < 0.05$).

samples were compared to hospital admission *venous* blood samples. No differences in blood concentrations of taurine were observed within the same time period (Kruskal–Wallis test) for those patients undergoing single or multiple grafts or valve replacements.

Blood drawn from eleven patients undergoing coronary artery bypass (Group I) surgery was chromatographed on the amino acid analyzer. Concentrations of certain amino acids and nonprotein substances differed significantly during the postoperative period when compared to arterial presurgery values. The ninhydrin positive substances, measured by the amino acid analyzer, are classified as follows: essential amino acids (Fig. 4): nonessential amino

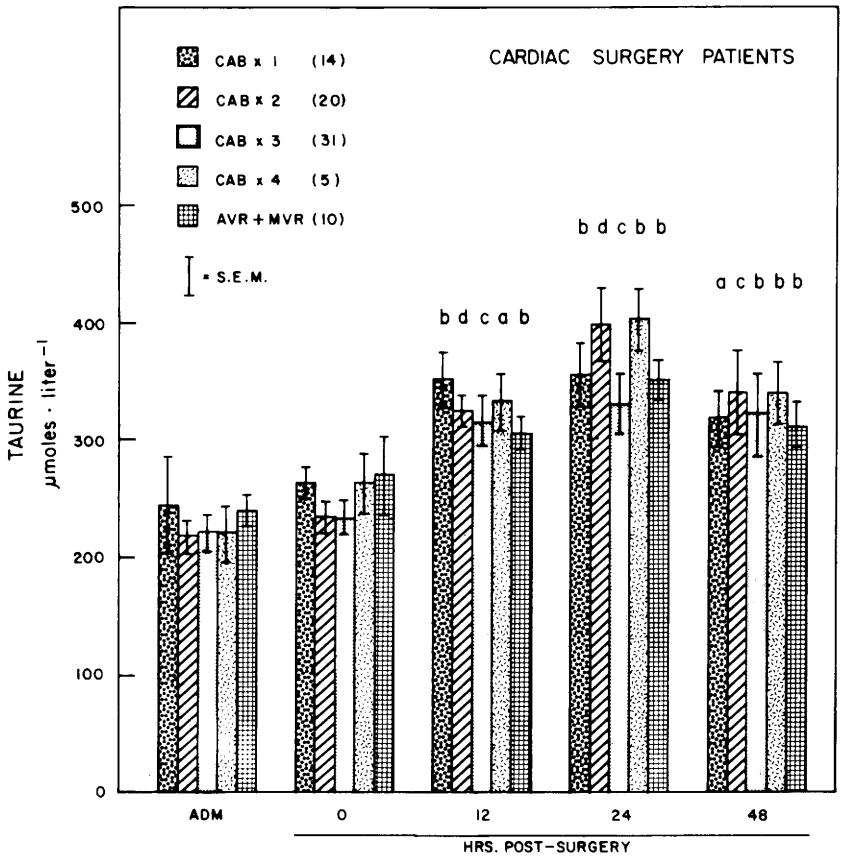

FIG. 3. Taurine concentrations in blood obtained from 80 patients undergoing cardiac surgery. Seventy coronary artery bypass (CAB) patients were classified as to the number of grafts received. Ten patients had either aortic (AVR) or mitral (MVR) valve replacements. *P* values ($^aP < 0.05$; $^bP < 0.02$; $^cP < 0.005$; $^dP < 0.001$) describe significant differences between admission (ADM) taurine values and postsurgery values at designated time periods.

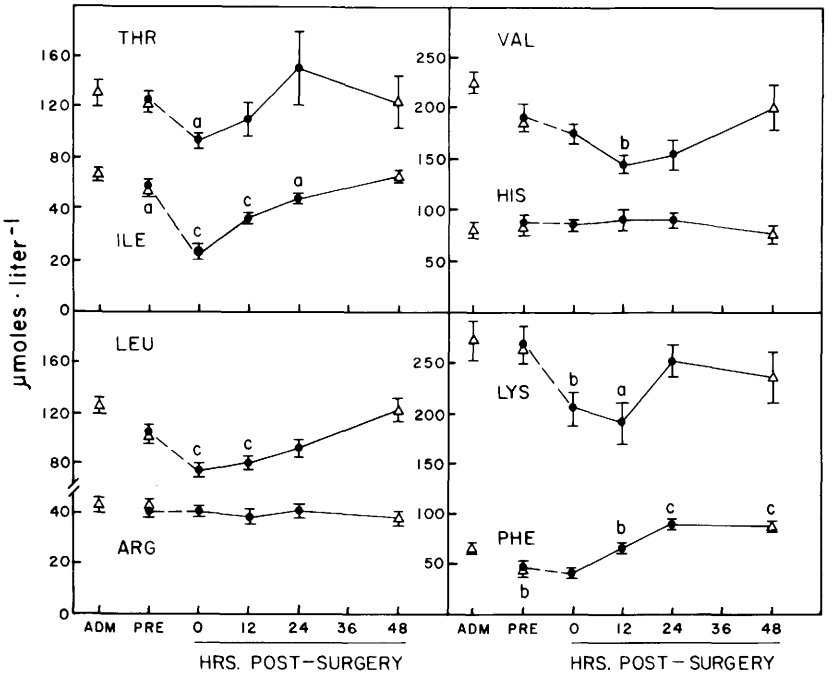

FIG. 4. Concentrations of essential amino acids in blood obtained from 11 patients undergoing coronary artery bypass surgery. Venous blood is designated by the open triangles; arterial blood is designated by closed circles. Letters representing P values placed above standard errors are comparisons between postsurgery blood values with presurgery (PRE) values. Letters placed below standard errors on presurgery (PRE) values are comparing this amino acid value with the value obtained on admission (ADM) blood. ($^aP < 0.05$; $^bP < 0.01$; $^cP < 0.001$).

acids (Fig. 5): nonprotein ninhydrin positive compounds (Fig. 6).

Analysis of amino acids and other ninhydrin positive nonprotein substances were also performed on both venous and arterial blood samples which were drawn immediately after induction of anesthesia (samples designated PRE) (Figs. 4–6). Only one amino acid, glutamate (Fig. 5), demonstrated a significant difference between the samples.

Interestingly, the levels of many of the ninhydrin positive compounds in blood samples obtained upon admission of the patients to the hospital (ADM) were higher than the venous presurgery samples (Figs. 4–6). This difference could not be attributed to overnight fasting of the patient before the surgical procedure as there were no differences noted in the individual amino acid contents of venous blood obtained from volunteers before and after fasting for 14–16 hr (data not presented).

Taurine levels were also measured after two other types of surgical procedures, aortofemoral bypasses (Group III) and repair of abdominal aneurysms (Group IV) (Fig. 7). In both situations blood taurine concentrations increased postoperatively with respect to the presurgical blood samples.

Discussion. It has been reported that plasma concentrations of individual amino acids fluctuate after surgical procedures (6–10). In studies involving patients undergoing open-heart surgery it has been demonstrated that concentrations of all plasma amino acids increased during the period of extracorporeal circulation (11, 12). However, there are no postoperative data on the effects of cardiovascular surgery on the content of taurine and other amino acids in whole blood.

An immediate concern in the postoperative care and recovery of patients undergoing major surgical procedures is the rec-

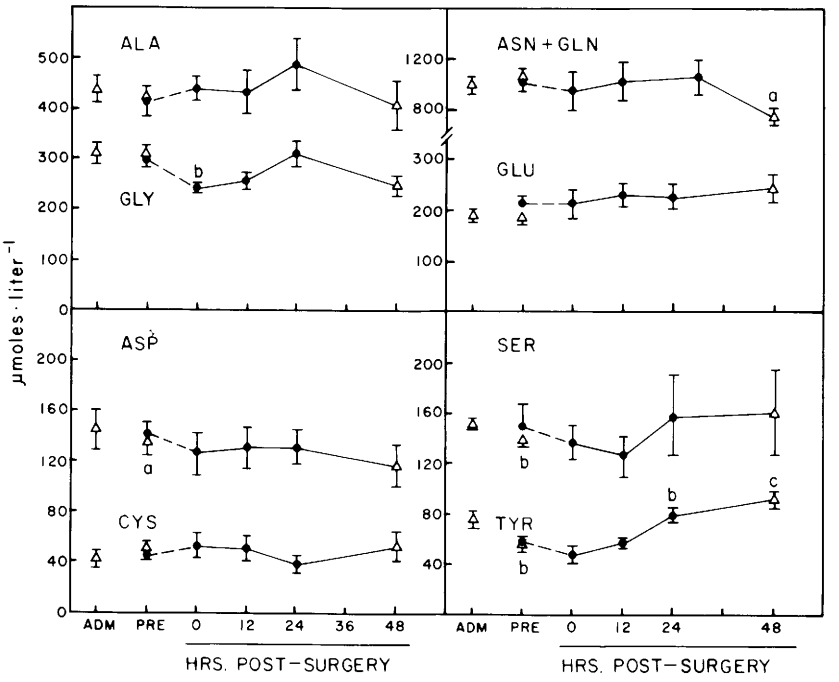

FIG. 5. Concentrations of non-essential amino acids in blood obtained from 11 patients undergoing coronary artery bypass surgery. Conditions of the experiment are described in the legend to Fig. 4.

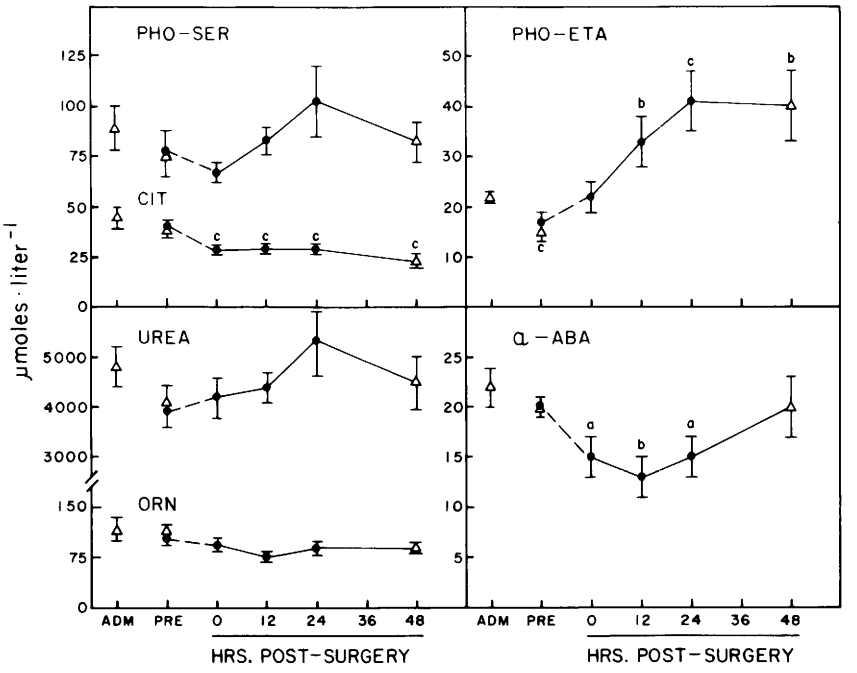

FIG. 6. Concentrations of nonprotein ninhydrin positive substances in blood obtained from 11 patients undergoing coronary artery bypass surgery. Conditions of the experiment are described in the legend to Fig. 4.

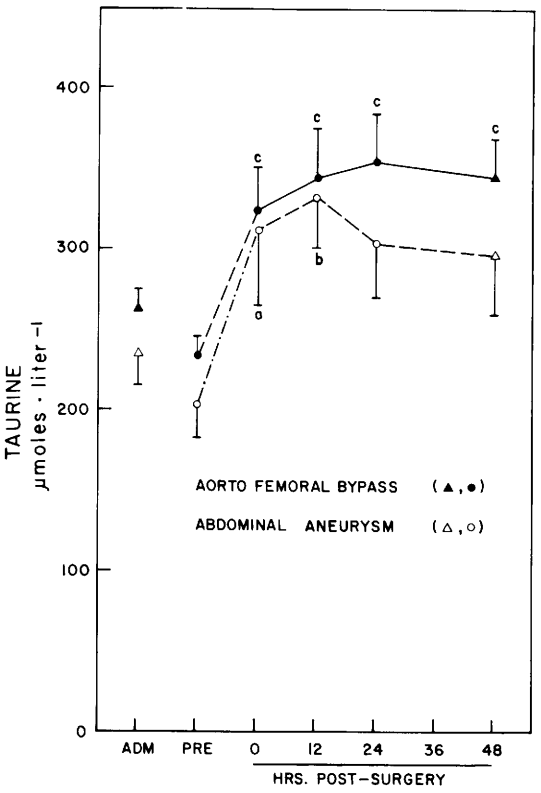

FIG. 7. Pre- and postoperative taurine concentrations in blood from seven patients undergoing aortofemoral bypass procedures and eight patients undergoing repair of abdominal aneurysms. Blood was drawn at the designated time periods. Arterial blood is designated by the symbols ○ or ●; venous blood is designated by △ or ▲. Data obtained on postsurgery blood samples are compared with presurgery (PRE) values. ($^aP < 0.05$; $^bP < 0.01$; $^cP < 0.005$).

ognition of the effects of trauma on the cardiovascular system. In previous studies in our laboratory it has been reported that taurine was released in significant quantities from the stressed or injured myocardium in animal models. Due to high levels in cardiac tissue (1) a role for taurine has ardently been sought. However, taurine has not yet been assigned a specific function in the myocardium. Evidence has suggested that taurine may have some role as a membrane stabilizer (13), an antiarrhythmic agent (14), or a modifier of calcium fluxes (15, 16). Taurine is released from myocardial tissue after coronary artery ligation in dogs (2), after perfusion of rat hearts in anoxic medium (3), and after administration of cardiotoxic quantities of the sympathomimetic agents, DL-isoproterenol and methoxamine, to rats (4). Taurine levels in blood increase after treatment with high doses of DL-isoproterenol or methoxamine in an inverse relationship to the loss of taurine content from cardiac tissue. However, it was not demonstrated in these experiments whether the increased taurine concentrations in the blood originated in the myocardium. In other studies utilizing patients admitted to the coronary care unit because of chest pain, it was observed that the concentrations of taurine increased in the blood of only those patients diagnosed as having had an acute myocardial infarction (5).

In the present study the levels of taurine also increased postoperatively in the blood of patients undergoing major surgical procedures such as coronary artery bypass, mitral or atrial valve replacements, femoral bypass, or repair of abdominal aneurysms. While it is tempting to speculate that the increase in blood taurine concentrations is due to myocardial damage in which cardiac cells release their contents, the incidence of direct cardiac damage in the coronary artery bypass patients was assumed to be low since the postoperative levels of the CPK-MB isoenzyme fraction were only 30.9 ± 7.7 and 23.6 ± 3.7 international units at 24 and 48 hr, respectively. It has been reported (17, 18) that transient low levels of CPK-MB isoenzyme can be determined in the plasma of many coronary artery bypass patients but only a very small percentage of these patients actually have an acute myocardial infarction diagnosed by both ECG abnormalities and significantly elevated CPK-MB isoenzyme fractions. In addition, taurine levels in our patients also increased after both aortofemoral bypass procedures and repair of abdominal aneurysms, procedures in which there is no manipulation of the heart. It is quite well-known that these types of major surgery (Group I–IV) produce severe stress in the patient which results in an increased secretion of epinephrine. Our results are thus consistent with the observation that sym-

pathomimetic agents raise blood taurine concentrations (4). Moreover, it has also been observed in our laboratory that administration of high doses of epinephrine to rats increase blood taurine levels while decreasing cardiac tissue content of taurine (Lombardini, unpublished data).

No correlations were observed between duration of anesthesia, extracorporeal circulation times (pump times), or aortic cross-clamping times with the CPK-MB isoenzyme fraction or blood taurine levels monitored at 24 and 48 hr after surgery. Moreover, no correlations were observed between the levels of CPK-MB isoenzyme and blood taurine at either 24 or 48 hr postsurgery.

The possibility was considered that the rise in taurine concentrations in blood was due to a reduced renal clearance following surgery. One of the primary routes of taurine excretion is by the kidneys (19) and it is well known that urine flow may be diminished after surgery. However, Turner and colleagues (20) reported that urinary excretion of taurine is increased two- to fourfold on the first postoperative day in patients after undergoing surgery for duodenal ulcers. Thus if kidney dysfunction was the cause of the increased blood taurine levels one would have expected the urinary taurine concentrations to decrease.

It has been previously reported that plasma taurine levels increased in severe battle wounds (7). Individual data were presented for two patients. The plasma level of taurine in the first patient was 76 μmole · liter^{-1} at 36 hr postinjury; the level of taurine in the second patient was 101 μmole · liter^{-1} at 12 hr postinjury. Normal values of plasma taurine were taken to be 48 μmole · liter^{-1}. It has also been reported that taurine levels in plasma decreased after surgical trauma both in patients (9) and animal models (10, 21). However, we observed that plasma levels did not change postoperatively but that whole blood levels did. Thus our results indicate that a cellular component(s) of blood sequestered taurine. It has been reported that platelets contain high quantities of taurine (22) and their capacity to transport taurine against a concentration gradient is well established (23, 24).

During the postsurgery period negative nitrogen balance is often encountered and the muscle mass may be reduced. These effects were expected in our series of patients. Previous reports (6, 8, 10) have shown that plasma amino acid concentrations are reduced immediately after surgery and we report herein that whole blood concentrations of the essential amino acids also decreased. This decrease is considered due to the utilization of these compounds by metabolic tissues. However, if there is a loss of amino acids from cellular components of whole blood to metabolic tissues then a regulatory process must be available to maintain the osmolarity of the cellular components. Taurine which functions as a osmoregulatory agent in lower vertebrates (25, 26) might be functioning in this role during the postoperative period.

Whether the effects we report in this paper are due to the anesthetic agents have been considered by other investigators (27). Dale and colleagues (27) reported that plasma amino acids changed after surgery but excluded anesthesia (sodium thiopentone/nitrous oxide/halothane) as the cause. On the contrary, Everson and Fritschel (6) demonstrated that the plasma essential amino acids were decreased in dogs by ether anesthesia. However, in our studies no tests were performed in animals to determine if the effect of anesthesia alone was responsible for our results.

Malnutrition has also been suggested as a contributing cause for the changes in plasma amino acids following surgery (8). However, Dale and colleagues (27) reported that when they divided their patients into two groups, one of which received 400 to 600 calories per day and the second group received 3000 calories per day, similar changes were observed in the postoperative concentrations of the plasma amino acids in both groups.

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