Thiol/Disulfide Redox Status Is Oxidized in Plasma and Small Intestinal and Colonic Mucosa of Rats with Inadequate Sulfur Amino Acid Intake

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ABSTRACT Low molecular weight thiol/disulfide redox pools are dependent upon extracellular cysteine (Cys) availability. We determined whether dietary sulfur amino acid (SAA) deficiency induces oxidative stress in vivo, as determined by redox state of major thiol/disulfide couples in plasma [Cys/cystine (CySS)] and intestinal mucosa [glutathione (GSH)/glutathione disulfide (GSSG)]. Rats were fed isocaloric, isonitrogenous semipurified diets: either SAA-adequate (control), SAA-deficient, or SAA-supplemented, pair-fed to intake of the SAA-deficient group. Reference rats consumed standard rat food ad libitum. After 7 d, plasma and gut mucosal samples were analyzed for Cys, CySS, GSH, and GSSG, and the redox potentials of Cys/CySS and GSH/GSSG were determined. Mean daily food intake in the pair-fed rats was similar (approximately one-half of reference-rat intake). Body weight decreased in all pair-fed groups, but rats fed the SAA-deficient diet lost significantly more body weight. Dietary SAA deficiency decreased GSH concentrations in both plasma and gut mucosa, increased plasma GSSG, and oxidized plasma and gut mucosal GSH/GSSG redox and plasma Cys/CySS redox. SAA supplementation resulted in a more reducing plasma Cys/CySS redox potential. Reference rats exhibited similar tissue and plasma GSH/GSSG redox as rats that ate semipurified SAA-adequate rat food, which provided similar net SAA intake. Our in vivo data show that inadequate dietary SAA intake oxidizes the thiol/disulfide redox status in rat-gut mucosa and plasma. Such oxidation of redox pools is associated with oxidative stress and the onset or progression of several pathological conditions. Thus, dietary SAA deficiency could contribute to the progression of disease by causing an oxidation of these components. J. Nutr. 136: 1242–1248, 2006.

KEY WORDS: • sulfur amino acids • redox • intestine

Cysteine (Cys)3 is a nonessential sulfur amino acid (SAA) and it plays a central role in cell function. Cys and its disulfide, cystine (CySS), are the predominant low molecular weight thiol/disulfide pool found in plasma and are central to the maintenance of the redox state of plasma proteins (1). In addition, Cys is utilized for protein and glutathione (GSH) synthesis and for synthesis of taurine and sulfate. These uses necessitate a constant nutritional intake of cysteine or its precursor, the essential SAA, methionine. Methionine is converted to the thiol homocysteine via S-adenosylmethionine and S-adenosylhomocysteine. GSH and sulfate function in detoxification, while taurine and sulfate are involved in diverse functions, including bile salt transport and osmotic regulation. Cysteine concentrations are maintained by an interorgan GSH/Cys cycle, dependent upon plasma membrane transport systems that balance cysteine availability among tissues and between the intracellular and plasma spaces (1,2). Extracellular Cys/CySS redox status has been implicated in cell growth and apoptosis, with cells more proliferative under reducing conditions (3), whereas cells grown in oxidizing conditions are more sensitive to oxidant-induced apoptosis (4). Depressed Cys levels in plasma and tissues have been observed in different disease states, including HIV infection (5), cirrhosis (6), and inflammatory bowel disease (7).

The GSH and GSH disulfide (GSSG) systems play a critical role in determining intracellular redox balance and antioxidant function (2). GSH that is in the gut lumen is required for normal intestinal function (8) because its antioxidant functions protect the lumen from damage by electrophiles (9,10) and maintain the sulfhydryl/disulfide balance of protein thiols (11). For example, depletion of GSH, induced by buthionine sulfoximine, results in a degeneration of jejunal and colonic epithelial cells in mice (8). Cys is continuously needed for GSH synthesis; therefore, dietary Cys deficiency could deleteriously affect intestinal functions, either directly or indirectly, by limiting plasma or mucosal GSH concentrations.
The concentration of L-cystine, L-methionine, L-alanine, L-aspartic acid, glycine and L-serine in the 3 semipurified diets was varied, as indicated, to formulate isocaloric, isonitrogenous pelleted diets that varied in SAA content. Diet content of all other amino acids was identical in the 3 diets (L-Arg 12.1, L-Asn 6.0, L-Glu 40.0, L-His 4.5, L-Ile 8.8, L-Leu 11.1, L-Lys 18.0, L-Phe 7.5, L-Pro 3.5, L-Thr 8.2, L-Trp 1.8, L-Tyr 5.0, and L-Val 8.2 g/kg diet, respectively). Macrom- and micronutrient content was also identical in the 3 diets and conformed to AIN-93 diet guidelines for rodents (18). The 3 diets contained (in g/kg diet): sucrose 352, corn starch 150, maltodextrin 150, soybean oil 80, cellulose 30, vitamin mix 13, mineral mix 35, calcium phosphate 8.2, choline bitartrate 2.5, and tert-butylhydroquinone 0.02, respectively. The vitamin and mineral mixes were AIN-93-VX and AIN-93M-MX, respectively (18).

The GSH pool is oxidized to GSSG during its function as an antioxidant, both in nonenzymatic and enzymatic reactions. GSH peroxidase is one enzymatic route for GSSG generation, while the other is glutaredoxin (Grx). GSH peroxidase uses GSH to reduce peroxides, generating GSSG in the process. Grx, on the other hand, reduces protein disulfides directly via its active site dithiol, which is then converted to a disulfide. GSH reduces Grx and, in the process, is oxidized to GSSG. GSSG thus generated is recycled to GSH by an NADPH-dependent GSSG reductase (12). The GSH/GSSG redox balance is therefore dependent on both GSSG reductase and NADPH, which serves as the electron donor for recycling GSH. NADPH generation is functionally coupled to the pentose phosphate pathway (13) and is regulated by energy supply in the form of glucose. Glucose stimulation of enterocyte NADPH supply (14) suggests that GSH redox cycle activity is dependent on exogenous glucose availability for NADPH production. Supporting this concept is evidence that glucose depletion decreases the elimination of luminal peroxidized lipids reminiscent of the GSH-deficient state (9,15). NADPH might, therefore, become limiting during energy restriction.

In vitro studies in human colonic epithelial cells show that deficiency of Cys in the culture medium is sufficient to cause oxidation of cellular GSH/GSSG redox; this is rapidly reversed with Cys repletion (16). In rats, both food deprivation and generalized dietary restriction (25% of ad libitum intake) led to GSH depletion and oxidation of small bowel and colonic GSH/GSSG redox (17). In that study, however, both food deprivation and food restriction resulted in depletion of micronutrients, energy, fat, and protein. Whether oxidation of gut mucosal GSH redox can be induced by dietary SAA deficiency alone is unknown.

The purpose of the present study is to determine the effects of dietary SAA deficiency and SAA supplementation on the redox status of Cys and GSH in plasma and the redox status of GSH in rat small bowel and colonic mucosa.

### MATERIALS AND METHODS

Male Sprague-Dawley rats (Charles River Laboratories), weighing 200–250 g, were housed in individual cages in the animal care facility under controlled conditions of temperature and humidity with a 12-h light (0700–1900) and 12-h dark (1900–0700) cycle. Rats had free access to water and were initially fed standard pelleted rat food (Laboratory Rodent Chow 5001, PMI Feeds) during a 7-d acclimation period. The study protocol was approved by the Institutional Animal Care and Use Committee of Emory University, Atlanta, GA.

**Study diets.** Semipurified diets were custom-prepared (Harlan-Teklad) to examine responses to SAA deficiency and SAA supplementation, respectively (Table 1). The study compared 3 groups of rats consuming the following diets: SAA adequate (control), SAA deficient, and SAA supplemented. A fourth group of rats were fed standard rat food (Laboratory Rodent Chow 5001, PMI Feeds) ad libitum and served as a reference group that was not included in the statistical analysis.

The amino acid content of the custom-prepared diets was formulated in consultation with Dr. R. Ross of Harlan-Teklad to avoid a markedly imbalanced amino acid profile in these isonitrogenous diets; and 2) provide amounts of methionine and CySS unlikely to induce food avoidance (i.e., inclusion of a small amount of methionine in the SAA-deficient diet and a 218% increase of total SAA in the SAA-supplemented diet compared with the SAA-deficient diet). The SAA and nitrogen concentrations were adjusted to the desired experimental levels by varying the amount of CySS, methionine, and the nonessential amino acids L-alanine, L-aspartic acid, glycine, and L-serine. The SAA-adequate semipurified control diet contained 11.7 g/kg of SAA (0.35% of diet as cysteine and 0.82% of

### TABLE 2

**Daily food intake, SAA intake, and body weight changes in rats fed diets containing various SAA concentrations**

<table>
<thead>
<tr>
<th>Group</th>
<th>Food intake, g/d</th>
<th>SAA intake, mg/d</th>
<th>Initial body weight, g</th>
<th>Body weight change, g/7 d</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAA-adequate</td>
<td>8.4 ± 0.8</td>
<td>98 ± 9g</td>
<td>214 ± 4</td>
<td>−0.4 ± 0.7b</td>
</tr>
<tr>
<td>SAA-deficient</td>
<td>8.6 ± 0.8</td>
<td>17 ± 9g</td>
<td>210 ± 3</td>
<td>−3.0 ± 0.6a</td>
</tr>
<tr>
<td>SAA-supplemented</td>
<td>8.4 ± 0.8</td>
<td>214 ± 9g</td>
<td>219 ± 3</td>
<td>−0.6 ± 0.6b</td>
</tr>
<tr>
<td>Standard rat chow</td>
<td>16.4 ± 0.1</td>
<td>123 ± 1</td>
<td>204 ± 3</td>
<td>5.8 ± 2.2</td>
</tr>
</tbody>
</table>

1. Values are means ± SE, n = 6. Means for the 3 groups fed semipurified diets with superscripts without a common letter differ, P < 0.05.
2. SAA, L-cystine + L-methionine.
3. Laboratory Rodent Chow 5001 (PMI Feeds) containing cysteine at 0.32% and methionine at 0.43% of diet, respectively.
diet as methionine). Ad libitum intake of the amino acid–modified diets was expected to be less than that of the standard rat food during the acclimation period. Thus, the SAA-adequate diet was custom-formulated to provide a greater SAA content (as a percentage of diet) compared with the amount of SAA present in the standard rat food (which provided 7.5 g/kg SAA). The SAA-deficient diet contained no CySS and 24% of the methionine content of the SAA-adequate control diet (17% of control diet SAA content). The SAA-supplemented diet contained 300% of the CySS content and 183% of the methionine content of the SAA-adequate diet, respectively (218% of control diet SAA content). The 3 semipurified diets were designed to be isocaloric and isonitrogenous and to contain adequate and identical quantities of energy, nitrogen, carbohydrate, fat, fiber, micronutrients, and essential amino acids (with the exception of SAA) (18) (Table 1). Tolerance of each of the semipurified diets was confirmed in pilot studies, indicating apparent palatability, although ad libitum intake was approximately one-half of the intake of rats fed standard rat food (data not shown).

Experimental design and operative procedures. The rationale for this design was to explicitly test the effect of variations in SAA intake on plasma and tissue thiol/disulfide redox state. The ad libitum-fed reference group was included to determine whether the unique features of the experimental conditions (SAA content, synthetic mixture of amino acids, palatability, and food intake) grossly altered redox characteristics relative to usual animal care conditions. A total of 24 rats were assigned to the 3 experimental groups fed the semi-purified experimental diets and the reference group (n = 6/group). The SAA-adequate (control) and SAA-supplemented groups were pair-fed to the mean daily food intake of the rats fed the SAA-deficient diet, as this group was shown in pilot studies to eat the least amount of food. Food was supplied to all groups between 1000 and 1100 h each morning, when the intake from the previous 24-h period was recorded. Timing of food intake during the 24-h periods was not determined. Body weight and food intake were determined daily for 7 d.

Tissue collection. After 7 d of consuming the diets, the rats were killed between 0900 and 1200 h after overnight food-deprivation. Blood was drawn by cardiac puncture and plasma processed as previously described (19). Defined segments of jejunum, ileum, and colon were stripped of mesenteric and vascular connections and sequentially removed from the peritoneum. The lumen was flushed with ice-cold saline to clear intestinal contents. The segments used for mucosal thiols studies were longitudinally cut and the mucosa obtained by gentle scraping with a glass slide. The mucosal samples were immediately placed in liquid nitrogen for further processing.

GSH, GSSG, Cys, and CySS determination. Gut mucosal samples were treated with ice-cold 5% (v:v) perchloric acid, containing 0.2 mol/L boric acid and 10 μmol/L γ-glutamyl-glutamate (internal standard),...
and precipitated tissue proteins were separated from the acid-soluble supernatant by centrifugation (17). The protein pellet was resuspended in 1 mol/L NaOH, and protein concentrations were measured using the Bradford method (18), with rabbit γ-globulin as the protein standard (Biorad Laboratories). Intracellular GSH and GSSG levels were determined following removal of perchloric acid, and treatment of the supernatant with iodoacetic acid was followed by dansyl derivatives of cysteine and cystine separated by HPLC (17,19).

**Calculations.** The tissue and plasma redox potential \( E_h \) values were calculated using the appropriate forms of the Nernst equation (mV) (20) for the respective GSH/GSSG and Cys/CySS pools: \( E_h = -64 + 30 \log ([GSSG]/[GSH]) \) for pH 7.4 in rat tissues and plasma (21) and \( E_h = -50 + 30 \log ([Cys]/[CySS]) \) for pH 7.4 in plasma, where respective concentrations are expressed in molarity.

**Statistical analysis.** Tests for statistically significant differences among the 3 pair-fed study groups were performed by one-way ANOVA, with post-hoc Fisher’s protected least-significant difference tests. Values are means ± SEM. Differences were considered significant at \( P < 0.05 \).

**RESULTS**

**Food intake and body weight.** Daily food intake was similar in the rats fed the semipurified diets with differing SAA content (Table 2). As designed, the daily SAA intake was markedly decreased in the group fed the SAA-deficient diet (to 17% of intake in the SAA-adequate diet group) and was increased in the SAA-supplemented group (214% of intake in the SAA-adequate diet group). The pair-fed rats ate approximately one-half of the intake of the reference rats. However, because the SAA content of the custom SAA-adequate diet was higher than that in the rat food fed to the reference rats, daily SAA intake by these 2 groups was similar (Table 2). Initial body weight among the groups was similar, but rats fed the SAA-deficient diet lost significantly more body weight than their pair-fed counterparts in the SAA-adequate and the SAA-supplemented groups. This catabolic response is likely due to deficiency of the essential amino acid methionine in the diet, coupled with decreased overall food intake. Reference rats ate approximately twice as much food as the rats fed semipurified diets and exhibited the expected weight gain. Our models of altered SAA intake were therefore evaluated on a background of protein-energy malnutrition.

**Plasma thiol/disulfide redox pools.** Dietary SAA deficiency caused a marked decrease in plasma Cys and CySS concentrations (Fig. 1A, B), leading to a significant oxidation of the Cys/CySS \( E_h \) (Fig. 1C) compared with the SAA-adequate and SAA-supplemented groups. Although the plasma CySS concentration in the SAA-deficient diet was less than the concentration in the SAA-adequate and SAA-supplemented groups (Fig. 1B), the proportion of total cyst(e)ine (Cys + CySS) present as CySS in the SAA-deficient was 3 times the proportion found in the SAA-adequate and SAA-deficient groups (13 compared with 4%; data not shown). Dietary supplementation of SAA resulted in a significant increase in plasma Cys concentration (Fig. 1A) compared with the SAA-adequate group and did not change CySS concentration (Fig. 1C). This increase in plasma Cys to values comparable to the reference group resulted in a significantly more reducing plasma Cys/CySS \( E_h \) versus the other 2 pair-fed groups. Reference rats had higher concentrations of both plasma Cys and CySS than the SAA-adequate group; however, the plasma Cys/CySS \( E_h \) was similar in these groups (see legend to Fig. 1).

Alteration of dietary SAA did not change plasma GSH concentrations (not shown). Depletion of SAA resulted in a marked increase in GSSG concentrations compared with values in rats fed similar SAA-adequate and SAA-supplemented diets (Fig. 2A). Plasma GSH/GSSG redox was oxidized in rats fed the SAA-deficient diet when compared with the SAA-adequate and SAA-supplemented groups (Fig. 2B). Reference rats had greater plasma GSH concentrations than the SAA-adequate group, but GSSG concentrations were similar to those in the
SAA-deficient group such that the GSH/GSSG redox was more oxidized than in the SAA-adequate rats (see legend to Fig. 2).

**Gut mucosal GSH and GSSG concentrations and GSH/GSSG redox potential.** SAA deficiency led to an oxidation of the GSH/GSSG redox pools in ileal, jejunal, and colonic mucosa when compared with the SAA-adequate and the SAA-supplemented groups. (Fig. 3). There was no difference in the jejunal, ileal, or colonic GSH/GSSG redox values between the SAA-adequate and the SAA-supplemented groups (Fig. 3). In all three intestinal tissues, the GSH/GSSG \( E_h \) values in the SAA-adequate and SAA-supplemented groups were similar to the reference group consuming standard rat chow ad libitum (see legend to Fig. 3). GSSG concentrations did not differ among the groups (Table 3). Thus, the oxidation of gut mucosal GSH/GSSG redox in rats fed the SAA-deficient diet was likely due to the significant decrease in GSH levels in gut mucosa compared with the other 2 experimental SAA groups (Table 3).

**DISCUSSION**

Previous studies have documented the effect of nutritional status on low molecular weight thiols and their disulfide and redox states in tissues. Decreased Cys and GSH concentrations have been observed in the plasma and erythrocytes of children with severe malnutrition (22,23), and oxidation of the GSH/GSSG redox state was demonstrated in the liver and spleen of protein-malnourished mice (24). Cys is a GSH precursor and is involved in the rate-limiting step for GSH synthesis; its deficiency has been shown in vitro to be sufficient to cause an oxidation of cellular GSH/GSSG redox potential of intestinal and retinal pigment epithelial cells (16,25). However, the specific effects of altered dietary SAA content on plasma and tissue redox potential is unknown. Thus, our study was designed to extend these previous findings to an in vivo nutritional model.

The present data show that, in adult rats, dietary SAA depletion (Tables 1, 2) in the setting of reduced overall food intake, compared with the intake of rats fed standard rat food (i.e., generalized nutrient depletion), is sufficient to cause oxidation of Cys/CySS redox in plasma. Our successful pair-feeding regimen indicates that the changes observed were a function of changes in dietary methionine and CySS intake (Table 2), and not of changes in dietary intake of micronutrients, energy, fat, nitrogen, or non-SAs. Plasma changes were due partly to a marked reduction of available Cys in the SAA-deficient group, when compared with the SAA-adequate group. The proportion of total cysteine (Cys + CySS) present as CySS was higher (3-fold) in the SAA-deficient group, when compared with the SAA-adequate and SAA-supplemented groups. Thus, although the concentration of CySS is lower for this group, proportionally, there was an increase in CySS levels for the SAA-deficient group, which contributed to the oxidation of the plasma Cys/CySS redox observed. Supplementation with SAA markedly increased plasma Cys concentrations compared with the other SAA groups, leading to a further reduction in the Cys/CySS \( E_h \) to values that were similar to those obtained in reference rats that ate twice as much in g/d of standard rat chow (Table 2). The effect of SAA deficiency on plasma GSH/GSSG redox also showed that this nutritional manipulation leads to an oxidation of this important redox couple when compared with the SAA-adequate group. Interestingly, SAA deficiency was associated with increased plasma GSSG concentrations. This could be due to decreased clearance from plasma or increased release of GSSG from tissues. However, the values for plasma GSH/GSSG redox for the SAA-depleted group were similar to those obtained in reference rats consuming standard rat chow. This observation is consistent with studies in healthy humans consuming a SAA-free diet in which blood GSH concentrations were maintained over a 10-d period (26). There was no difference in the plasma GSH/GSSG redox between the SAA-adequate and the SAA-supplemented groups, but \( E_h \) values for these groups were more reduced than in the pair-fed rats consuming the SAA-deficient diet. This shows that SAA regulates the plasma GSH/GSSG redox potential; however, consuming diets supplemented with SAA does not further reduce systemic GSH/GSSG redox.

In the intestinal mucosa, we demonstrated that SAA depletion oxidizes the GSH/GSSG redox potential in jejenum, ileum, and colon. Jonas et al. (17) showed that both fasting and refeeding at 25% ad libitum food intake after a 3-d fast led to an oxidized GSH/GSSG pool in gut tissues. Our previous nutritional models incorporated deficiency of all other nutritional components. The current data extend these earlier studies by demonstrating the specific effects of altered dietary SAA intake on plasma and gut mucosal GSH and CySS redox.

Supplementing with SAA did not improve gut mucosal GSH/GSSG redox when compared with the SAA-adequate diet. Other studies have demonstrated restoration of tissue GSH as well as GSH/GSSG redox with Cys prodrugs such as N-acetyl cysteine, methionine, and L-2-oxo-4-thiazolidine-carboxylate (23,24,27). In these studies, effects were seen in situations where the GSH/GSSG redox had already been compromised by either protein malnutrition or age. Moreover, in the studies where changes were seen in tissue GSH/GSSG redox state in response to Cys prodrugs (24), no effects were observed in the colon, indicating that effects of these agents may be tissue

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**TABLE 3**

<table>
<thead>
<tr>
<th></th>
<th>Jejunum</th>
<th>Ileum</th>
<th>Colon</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>GSH</td>
<td>GSSG</td>
<td>GSH</td>
</tr>
<tr>
<td>SAA-adequate</td>
<td>20.9 ± 1.3\a</td>
<td>0.24 ± 0.03</td>
<td>20.5 ± 0.06\a</td>
</tr>
<tr>
<td>SAA-deficient</td>
<td>14.6 ± 1.7\a</td>
<td>0.27 ± 0.03</td>
<td>11.2 ± 1.2\a</td>
</tr>
<tr>
<td>SAA-supplemented</td>
<td>20.2 ± 1.1\a</td>
<td>0.19 ± 0.08</td>
<td>18.1 ± 2.5\a</td>
</tr>
<tr>
<td>Standard rat chow (reference)</td>
<td>18.0 ± 1.2</td>
<td>0.23 ± 0.03</td>
<td>18.9 ± 2.5</td>
</tr>
</tbody>
</table>

1 Values are means ± SE, \( n = 6 \). Means for the 3 groups fed semipurified diets with superscripts without a common letter differ, \( P < 0.05 \).
specific. Also, although the drugs restored GSH levels in the liver, lung, heart, and spleen, redox status was only restored in the liver and heart, suggesting that restoration of GSH and restoration of GSH/GSSG redox is not necessarily concomitant. In our models, plasma and tissue GSH/GSSG redox changes may be maximal for the level of diet consumed and unable to become more reducing with SAA supplementation alone. The pair-feeding regimen we used required that rats be pair-fed to the group with the lowest ad libitum food intake (SAA-deficient group). As this group of rats ate approximately one-half of the food intake of the reference chow-fed rats (Table 2), additional studies, using enteral tube feeding of liquid diets to provide the higher energy/protein-amino acid intake required for animal growth, would be of interest to determine whether the effects of the altered SAA intakes we observed are altered as a function of changes in overall dietary intake. Determining tissue redox in rats fed less limiting SAA diets that enable some somatic growth would also be of interest. Whether the relations between SAA intake and plasma versus gut mucosal Cys/CySS and GSH/GSSG redox, are altered in specific disease states or are a function of kinetics of GSH conversion to GSSG, regulation of SAA transport systems, or tissue SAA/GSH output, are also of interest and require further study.

From the dietary standpoint, SAAs are readily available in animal protein, but are present in lower amounts in fruits, vegetables, and grains (28,29). Also, lifestyle choices, such as smoking, chronic alcohol consumption, and exercise, as well as clinical conditions, such as HIV infection, gut mucosal inflammation, and other catabolic conditions, may lead to depletion of tissue and plasma GSH or Cys levels (5–7,30–33). In the current study, rats were fed their respective diets for a 1-wk period. Decreased palatability or other factors of the SAA-deficient diet resulted in lower food consumption in rats fed these semipurified SAA diets than reference rats fed standard rat chow (Table 2). Thus, the needed pair-feeding regimen that enabled us to test our hypotheses resulted in a lower amount of total diet intake than reference rats, which was the likely reason for lack of weight gain in all nonreference groups over time as compared with the reference group. Differences in the timing of food intake within the pair-fed group, or between the pair-fed and ad libitum reference group, could have influenced our results (e.g., nibbling versus foodate during the dark cycle). Such data were not determined but would be of interest in future studies. Our data suggest that, in the setting of an overall decrease in consumption of a mixed diet, the level of SAA intake can markedly alter the redox status of both Cys/CySS (the major plasma redox pool) and GSH/GSSG (the major redox pool in tissues). Our data have relevance because oxidation of these redox indices has been associated with disease (5–7) and aging (34,35). Also, oxidation of both extracellular Cys/CySS and cellular GSH/GSSG redox has been shown to sensitize cells to oxidant-induced injury (4,36,37). The present results therefore suggest that inadequate dietary SAA intake, by oxidizing plasma and tissue redox pools, may contribute to the onset or progression of diseases influenced by redox status. Further studies on the potential effects of altered SAA intake on morphology and function of the gut mucosa and other tissues in models of stress, malnutrition, or nutrient repletion are necessary to test these hypotheses.

LITERATURE CITED


