First-pass splanchnic metabolism of dietary cysteine in weanling pigs

C. Bauchart-Thevret, J. Cottrell, B. Stoll, and D. G. Burrin

Department of Pediatrics, USDA/ARS Children’s Nutrition Research Center, Baylor College of Medicine, Houston, TX 77030

ABSTRACT: Cysteine is a semi-indispensable AA in neonates and is synthesized from the indispensable AA, methionine, by transsulfuration. We previously showed that the gastrointestinal tract (GIT) is a metabolically important site of methionine transsulfuration to cysteine, yet the metabolic fate of dietary cysteine in the GIT has not been established. Cysteine use by gut epithelial cells may play an important role for maintenance of glutathione synthesis and cellular redox function. Our aim was to quantify the extent of gastrointestinal first-pass cysteine metabolism in young pigs. Four-week-old weanling pigs (n = 10) were fed a liquid milk-replacer diet and given an intragastric and intravenous [1-13C]cysteine infusion on 2 separate days in a crossover design. Arterial and portal blood samples were collected for cysteine isotopic enrichment by gas chromatography-mass spectrometry and for 13CO2 enrichment by isotope ratio mass spectrometry. Our results indicated that dietary cysteine is metabolized during its first-pass splanchnic metabolism, accounting for about 40% of dietary cysteine intake. We also showed that intestinal absorption was the major metabolic fate of dietary cysteine, representing about 75% of intake, indicating that the GIT utilizes 25% of the dietary cysteine intake. Thus, utilization by the GIT represents about one-half (approximately 53%) of the first-pass, splanchnic uptake of dietary cysteine. Moreover, a substantial proportion of dietary splanchnic cysteine metabolism was consumed by the GIT via nonoxidative pathways. We conclude that the gut utilizes 25% of the dietary cysteine intake and that synthesis of mucosal epithelial proteins, such as glutathione and mucin, are a major nonoxidative metabolic fate for cysteine.

Key words: glutathione, gut, sulfur amino acid, transsulfuration

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INTRODUCTION

Cysteine is a sulfur AA (SAA) present in dietary proteins, but is also synthesized from the indispensable AA methionine by transsulfuration, an irreversible process (Stipanuk, 2004). Thus, dietary cysteine can satisfy a portion of the SAA (methionine, cysteine, and cystine) requirement, the so-called cysteine sparing effect on the dietary methionine requirement (Ball et al., 2006). Many studies performed on animals have indeed shown that more than 40% of the SAA requirement can be met by dietary cysteine by reducing methionine catabolism through the transsulfuration pathway (Shoveller et al., 2003; Baker, 2006; Ball et al., 2006). Although the liver is usually considered the major site of SAA metabolism (Stipanuk, 2004), we have shown that the intestine also plays an important role in this regard. In infant piglets, we showed that the gastrointestinal tract (GIT) metabolizes about 20% of dietary methionine intake, which is converted via transmethylating to homocysteine and transsulfuration to cysteine (Riedijk et al., 2007). We also determined that the GIT accounts for about 25% of whole-body transmethylating and transsulfuration (Riedijk et al., 2007). However, the metabolic fate of dietary cysteine in the GIT has not been described in detail.

Previous reports in pigs indicate that only approximately 20% of dietary cysteine appears in the portal blood, indicating extensive first-pass GIT metabolism of cysteine (Rérat et al., 1992; Bos et al., 2003). Moreover, a recent study in minipigs reported that 40% of dietary cysteine is taken up by the GIT during its first-pass metabolism (Rémont et al., 2011). Therefore, the

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2Present address: Phosphagenics, 11 Duerdin St., Clayton, Victoria 3162, Australia.

3Corresponding author: dburrin@bcm.edu

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aim of the current study was to quantify the splanchnic metabolic fate of dietary cysteine metabolism in young pigs using a dual-stable isotopic tracer approach. The results of this study may further elucidate the role of the gut on the systemic bioavailability of dietary cysteine in young pigs and provide relevance to the nutritional needs of suckling and weanling pigs.

**MATERIALS AND METHODS**

The study protocol was approved by the Animal Care and Use Committee of Baylor College of Medicine and was conducted in accordance with the National Institutes of Health guidelines.

**Animals and Study Design**

The study was performed with 4-wk-old, female crossbred piglets (Large White × Hampshire × Duroc) obtained from the Texas Department of Criminal Justice (Huntsville, TX). The piglets arrived at the Children’s Nutrition Research Center in Houston at 14 d of age, and were fed a liquid milk replacement formula (Litter Life, Merrick’s Inc., Middleton, WI) at a rate of 50 mL·kg⁻¹·d⁻¹ for 7 d, which provided 25 g of lactose, 5 g of fat, and 12.5 g of protein per kilogram of BW daily. Cystine content was 0.61% of the diet, providing 5 g of fat, and 12.5 g of protein per kilogram of BW daily. At 21 d of age, after overnight food deprivation, piglets were surgically implanted with silastic catheters in the external jugular vein, carotid artery, portal vein, and stomach under isoflurane general anesthesia, as described previously (Burrin et al., 2000; Lambert et al., 2006). Piglets also were implanted with an ultrasonic flow probe (8 to 10 S model, Transonics, Ithaca, NY) around the portal vein. Postoperatively, they were placed on total parenteral nutrition, which provided elemental nutrients (glucose, AA, lipids, electrolytes, trace minerals, and vitamins) via continuous intravenous infusion at 5 mL·kg⁻¹·h⁻¹ for 24 h, as described previously (Burrin et al., 2000). Pigs were then enterally fed the liquid milk replacer formula (Litter Life, Merrick’s Inc.) at 10 mL·kg⁻¹·h⁻¹ in 4 feedings per day given in stainless-steel feeders; this recovery period was for 7 d before starting the infusion protocol.

**Infusion and Sampling Protocol**

At 28 d of age, all pigs (n = 10) received a primed (5 μmol/kg), continuous intravenous 2 h infusion (5 μmol·kg⁻¹·h⁻¹) of sodium-[¹³C]bicarbonate [NaH¹³CO₃], 99% atom percent excess (APE); Cambridge Isotope Laboratories, Andover, MA) for estimation of whole-body CO₂ production. Immediately thereafter, they received a primed (15 μmol/kg), continuous 6 h infusion (15 μmol·kg⁻¹·h⁻¹) of [¹³C]cysteine (99% APE; Cambridge Isotope Laboratories) administered either intragastrically (IG) or intravenously (IV) in a randomized, crossover design. Arterial blood samples (1 mL) were collected at 0, 1.5, 1.75, 6, 7, and 8 h in evacuated tubes, which contained 0.5 mL of cold 10% perchloric acid to release CO₂ for determination of [¹³C]CO₂ enrichment by isotope ratio-mass spectrometry. Arterial and portal blood samples (2 mL) were also collected at 0, 6, 7, and 8 h in EDTA-tubes, and plasma was immediately separated from erythrocytes by centrifugation (10 min at 2,000 × g at 4°C), snap-frozen in liquid nitrogen, and stored at −70°C until analysis for cysteine isotopic enrichment and cysteine concentration by gas chromatography-mass spectrometry (GC-MS). Hematocrit (Hct) was determined in all arterial and portal blood samples using a microcapillary reader after centrifugation (14,000 × g for 1 min at room temperature). Portal blood flow was monitored continuously throughout the infusion protocol via transit-time ultrasound. During the infusion, all pigs were intragastrically fed a bolus meal for 1 h that supplied 1/12th of the preceding total intake after an overnight fast, followed by a constant infusion at the rate of 10 mL·kg⁻¹·h⁻¹.

One or 2 d later, all pigs were subjected to the same infusion protocol but with a switch in their route of the tracer infusion, so that each pig received both an IG and IV infusion of [¹³C]cysteine at the end of the experiment to estimate the whole-body cysteine kinetics regarding the route of infusion. At the end of the second infusion day, all pigs were euthanized with an intravenous injection of sodium pentobarbital (50 mg/kg) and sodium phenytoin (5 mg/kg; Beutanasia-D, Schering-Plough Animal Health, Kenilworth, NJ).

**Mass Spectrometry**

Plasma isotopic enrichments of [¹³C]cysteine were quantified on heptafluorobutyric anhydride derivatives by GC-MS using a modified method from Davis et al. (2004). Briefly, plasma samples were acidified with 10% trichloroacetic acid, and AA were separated by cation exchange (AG 50W-X8, 100–200 mesh, hydrogen form resin, Bio-Rad, Richmond, CA), treated with dithiothreitol (Sigma-Aldrich, St. Louis, MO), and derivatized with heptafluorobutyric anhydride. The GC-MS analysis was performed by negative chemical ionization using a HP-5ms column (30 m in length, 0.25 mm i.d., 0.5 μm film thickness; Agilent Technologies, Palo Alto, CA). The abundance of specific ions was determined by selected-ion monitoring at the mass-to-charge (m/z) ratio 335 for cysteine [M + 0] and 336 for [L-¹³C]cysteine [M + 1]. Isotopic enrichments were expressed as molar percent excess (MPE) of labeled to nonlabeled isotopomer ratios (TTR, tracer/tracee ratios) after correction for natural abundance and standard curves, where MPE = [(TTR/(TTR + 1))] × 100 as defined by Wolfe and Chinkes (2005). Blood [¹³C]CO₂ enrichment was determined by isotope ratio-mass spectrometry as described previously (van Goudoever et al., 2000).
**Plasma Cysteine Concentrations**

Arterial and portal plasma cysteine concentrations were determined by isotopic dilution using GC-MS analysis after adding 20 μmol/L of [U-13C; 15N]-cysteine to plasma samples. Plasma samples were analyzed by GC-MS as described before by monitoring another specific ion at m/z 339 for [U-13C; 15N]-cysteine [M + 4]. Plasma cysteine concentration was calculated based on the abundance of natural cysteine [M + 0] and [U-13C; 15N]cysteine [M + 4] and corrected with standard curves.

**Whole-Body Cysteine Kinetics**

Whole-body cysteine kinetics were calculated using the mean of arterial plasma cysteine isotopic enrichments (expressed as MPE) for the 6- to 8-h time points where the steady-state was achieved during both IG and IV tracer infusions.

Whole-body [1-13C]cysteine flux (Q) in micromoles-kilogram⁻¹-hour⁻¹ was calculated as follows:

\[
Q = IR \times \left(\frac{IE_{\text{infusate}}}{IE_{\text{plasma}}} - 1\right),
\]

where IR is the [1-13C]cysteine tracer infusion rate (μmol·kg⁻¹·h⁻¹), and IE_{infusate} and IE_{plasma} are the isotopic enrichments (expressed as MPE) of the infused tracer and arterial plasma [1-13C]cysteine.

Whole-body CO₂ production (VCO₂) in micromoles-kilogram⁻¹-hour⁻¹ was calculated as follows:

\[
VCO₂ = IR \times \left(\frac{IE_{\text{infusate}}}{IE_{13CO₂}} - 1\right),
\]

where VCO₂ is the [1-13C]cysteine flux in micromoles-kilogram⁻¹-hour⁻¹ during the NaH13CO₃ infusion.

Whole-body 13CO₂ production (V13CO₂) in micromoles-kilogram⁻¹-hour⁻¹ was calculated as follows:

\[
V_{13CO₂} = VCO₂ \times IE_{13CO₂},
\]

Whole-body nonoxidative cysteine disposal into protein in micromoles-kilogram⁻¹-hour⁻¹ as an indicator of whole-body protein synthesis (PS) was calculated as follows:

\[
PS = Q - Ox.
\]

Whole-body cysteine balance in micromoles-kilogram⁻¹-hour⁻¹ was calculated as follows:

\[
\text{cysteine balance} = PS - PL.
\]

**Splanchnic [1-13C]Cysteine Utilization**

A portion of the IG tracer was utilized by the splanchnic tissues in the first pass and was not sampled in the blood. Therefore, first-pass splanchnic cysteine utilization in micromoles-kilogram⁻¹-hour⁻¹ was calculated as follows:

\[
\text{first-pass splanchnic cysteine utilization} = \left(\frac{Q_{\text{IG}} - Q_{\text{IV}}}{Q_{\text{IG}}}\right) \times I,
\]

where Q_{IG} and Q_{IV} are the whole-body [1-13C]cysteine flux in micromoles-kilogram⁻¹-hour⁻¹ during the IG and IV [1-13C]cysteine infusions, respectively, and I is the cysteine intake and was estimated at 107 μmol·kg⁻¹·h⁻¹.

**GIT Cysteine Mass Balance**

Plasma portal blood flow (PBF) in liters-kilogram⁻¹-hour⁻¹, after correction with Hct (%), was calculated as follows:

\[
PBF = PBF (mL/min) \times \left(\frac{60}{1,000}\right) \times \left(\frac{1}{\text{BW}}\right) \times \left(1 - \left(\frac{\text{Hct}}{100}\right)\right),
\]

where BW is the BW of each animal in kilograms at the time of the measurement.

Arterial cysteine input in micromoles-kilogram⁻¹-hour⁻¹ was calculated as follows:

\[
\text{arterial cysteine input} = [\text{Cys}]_{\text{art}} \times \text{PBF},
\]
where $[\text{Cys}]_{\text{art}}$ is the arterial plasma cysteine concentration in micromoles per liter and PBF is the plasma portal blood flow in liters·kilogram$^{-1}$·hour$^{-1}$ after correction with Hct. Portal cysteine output in micromoles·kilogram$^{-1}$·hour$^{-1}$ was calculated as follows:

$$\text{portal cysteine output} = [\text{Cys}]_{\text{port}} \times \text{PBF},$$

where $[\text{Cys}]_{\text{port}}$ is the portal plasma cysteine concentration in micromoles per liter.

The GIT cysteine absorption in micromoles·kilogram$^{-1}$·hour$^{-1}$ was calculated as follows:

$$\text{GIT cysteine absorption} = ([\text{Cys}]_{\text{port}} - [\text{Cys}]_{\text{art}}) \times \text{PBF},$$

Net GIT cysteine utilization in micromoles·kilogram$^{-1}$·hour$^{-1}$ was calculated as follows:

$$\text{net GIT cysteine utilization} = I - \text{GIT cysteine absorption},$$

where $I$ is the cysteine intake and was estimated at 107 μmol·kg$^{-1}$·h$^{-1}$.

**Statistics**

All data are expressed as means ± SE. The comparison between IG and IV values was performed with the 2-tailed Student’s $t$-test for paired data. Statistical significance was assigned at $P < 0.05$.

**RESULTS**

**Steady-State [1-$^{13}$C]Cysteine Enrichments**

Plateau isotopic enrichments were calculated as the mean of arterial plasma isotopic enrichments between 4 and 6 h of [1-$^{13}$C]cysteine infusion where the steady-state was achieved during both IG and IV tracer infusions (Figure 1A). Steady-state arterial [1-$^{13}$C]cysteine enrichments were less ($-39\%$) during the IG tracer infusion than in the IV tracer infusion (Figure 1B).

**Whole-Body Cysteine Metabolism**

Whole-body cysteine oxidation is depicted in Figure 2. Although the whole-body CO$_2$ production was not different between the 2 infusion groups (Figure 2A), the whole-body $^{13}$CO$_2$ production was greater ($+46\%$, $P < 0.01$) in the IV vs. IG group (Figure 2B), representing 32% of the [1-$^{13}$C]cysteine tracer infused during the IV infusion vs. 21% in the IG infusion (Figure 2C).

**Figure 1.** A) Time course and B) steady-state [1-$^{13}$C]cysteine enrichments (mole percent excess, MPE) in arterial plasma of 4-wk-old pigs receiving an intragastric (IG) or intravenous (IV) infusion of [1-$^{13}$C]cysteine. Data are means ± SE, $n = 10$ group. ***$P < 0.001$ (IG vs. IV).

**Figure 2.** Whole-body cysteine oxidation in 4-wk-old pigs receiving an intragastric (IG) or intravenous (IV) infusion of [1-$^{13}$C]cysteine. A) Whole-body CO$_2$ production, B) whole-body $^{13}$CO$_2$ production, C) fractional whole-body [1-$^{13}$C]cysteine oxidation of tracer infused, and D) whole-body [1-$^{13}$C]cysteine oxidation. Data are means ± SE, $n = 10$ group. **$P < 0.01$ (IG vs. IV).
However, no differences were found in whole-body [1-13C]cysteine oxidation rates between IG and IV groups (Figure 2D).

Whole-body cysteine fluxes are depicted in Figure 3. The whole-body [1-13C]cysteine flux was less (−41%, P < 0.001) in the IV vs. IG group (Figure 3A). The whole-body cysteine disposal into protein (i.e., protein synthesis; Figure 3B), and cysteine appearance from protein (i.e., proteolysis; Figure 3C), was substantially greater (P < 0.001) in IG compared with the IV group, which mainly reflects splanchnic uptake of the IG [1-13C]cysteine tracer. However, the whole-body cysteine balance was not different between the 2 groups (Figure 3D).

From the whole-body IV and IG tracer flux, it was determined that splanchnic tissues used 39% of the dietary cysteine intake in the first pass (Figure 4). Because both IV and IG groups received identical dietary intake via the IG cannula, arterial and portal cysteine concentrations and portal blood flow were equivalent (Table 1). The net GIT cysteine absorption was not statistically different depending on the route of tracer infusion, but represented 74% of dietary cysteine intake. We estimated the partitioning of dietary cysteine metabolism between the splanchnic organs, namely GIT and liver. Using the fractional first-pass splanchnic uptake (0.39), we determined the absolute amount of dietary cysteine intake (107 μmol·kg⁻¹·h⁻¹) used in the first pass by the splanchnic tissues and the GIT to be 41.7 μmol·kg⁻¹·h⁻¹ and 22.3 μmol·kg⁻¹·h⁻¹, respectively. The GIT accounted for approximately 53% of the first-pass splanchnic metabolism of dietary cysteine in young pigs (Figure 4).

### Table 1. Dietary cysteine intake and GIT cysteine mass balance in 4-wk-old pigs receiving an intragastric (IG) or intravenous (IV) infusion of [1-13C]cysteine

<table>
<thead>
<tr>
<th>Item</th>
<th>IG</th>
<th>IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dietary cysteine intake, μmol·kg⁻¹·h⁻¹</td>
<td>107</td>
<td>107</td>
</tr>
<tr>
<td>Arterial cysteine concentration, μmol/L</td>
<td>214 ± 16</td>
<td>212 ± 19</td>
</tr>
<tr>
<td>Portal cysteine concentration, μmol/L</td>
<td>233 ± 22</td>
<td>246 ± 21</td>
</tr>
<tr>
<td>Portal plasma flow, L·kg⁻¹·h⁻¹</td>
<td>2.70 ± 0.20</td>
<td>2.87 ± 0.20</td>
</tr>
<tr>
<td>GIT cysteine absorption, μmol·kg⁻¹·h⁻¹</td>
<td>79.5 ± 14.3</td>
<td>88.1 ± 18.2</td>
</tr>
<tr>
<td>% of intake</td>
<td>74.3 ± 13.4</td>
<td>82.4 ± 17.0</td>
</tr>
<tr>
<td>GIT cysteine utilization, μmol·kg⁻¹·h⁻¹</td>
<td>27.5 ± 14.3</td>
<td>18.9 ± 18.2</td>
</tr>
<tr>
<td>% of intake</td>
<td>25.7 ± 13.4</td>
<td>17.6 ± 17.0</td>
</tr>
</tbody>
</table>

Data are means ± SE, n = 10/group.

### Splanchnic and GIT Cysteine Metabolism

Splanchnic and GIT Cysteine Metabolism

Figure 3. Whole-body cysteine fluxes in 4-wk-old pigs receiving an intragastric (IG) or intravenous (IV) infusion of [1-13C]cysteine. A) Whole-body [1-13C]cysteine flux, B) whole-body protein synthesis, C) whole-body proteolysis, and D) whole-body cysteine balance. Data are means ± SE, n = 10/group. ***P < 0.001 (IG vs. IV).

Figure 4. First-pass splanchnic cysteine utilization in 4-wk-old pigs receiving an intragastric infusion of [1-13C]cysteine. GIT: gastrointestinal tract.
DISCUSSION

The main objective of this study was to quantify the metabolic fate of cysteine in the splanchnic area of 4-wk-old piglets by using a dual-tracer, IV and IG tracer isotopic approach combined with a portal balance approach. The splanchnic area comprises the portal-drained viscera that constitute the GIT and the liver. Although the liver is one of the major organs in the body that metabolizes SAA, increasing evidence indicates that the GIT, especially the intestine, is a metabolically important site of SAA metabolism. We previously demonstrated in infant piglets that the GIT metabolizes about 20% of the dietary methionine intake, which is mainly transmethylated to homocysteine and to cysteine by transsulfuration (Riedijk et al., 2007). Moreover, we recently showed that SAA deficiency substantially suppresses intestinal mucosal growth and reduces intestinal epithelial cell proliferation, and increases intestinal oxidative stress in piglets (Bauchart-Thevret et al., 2009). These findings emphasize the nutritional importance of intestinal metabolism of methionine and cysteine for intestinal mucosal growth and function.

In the present study, our results indicated that dietary cysteine is substantially metabolized during its first-pass splanchnic metabolism, accounting for approximately 40% of dietary cysteine intake. This is consistent with the decrease (−39%) in cysteine isotopic enrichments in arterial plasma during the IG infusion compared with the IV infusion, along with the decrease (−41%) in whole-body [1,15C]cysteine flux in the IV vs. IG group. This finding is in accordance with a recent study performed in adult minipigs that reported that 60% of dietary cysteine intake is absorbed by the GIT, indicating that 40% of dietary cysteine intake is sequestered by the gut (Rémont et al., 2011). Although the whole-body cysteine oxidation was not statistically different between the 2 groups, we found a greater fractional whole-body oxidation of parenteral cysteine (IV, 32%) than enteral cysteine (IG, 21%), indicating a greater systemic than splanchnic oxidation of cysteine. Based on the distribution of cysteine dioxygenase (CDO), the rate-limiting enzyme for cysteine oxidation as a guide for the sites of cysteine oxidation, it would seem that the kidney and lung are the primary sites for cysteine oxidation outside of the splanchnic bed (Hirschberger et al., 2001). Within the splanchnic bed, the liver is by far the primary site of CDO expression. However CDO is found in mucus-secreting goblet cells and pancreatic exocrine cells (Stipanuk et al., 2009). We also demonstrated that intestinal absorption was the major metabolic fate of dietary cysteine, representing about 75% of intake, indicating that the GIT uses about 25% of the dietary cysteine intake and about 53% of the splanchnic first-pass uptake. In addition to substantial utilization of dietary cysteine, we have previously shown that the GIT is a substantial site of endogenous cysteine synthesis; about 23% of the whole-body transsulfuration occurred in the GIT and one-third of all methionine used by the gut was used for cysteine synthesis (Riedijk et al., 2007).

Our findings indicate that the GIT uses a substantial proportion of dietary splanchnic cysteine for nonoxidative purposes, most likely synthesis of proteins such as glutathione, as has been observed in vivo in rodent studies after intravenous infusion of 15N-cysteine (Malmezat et al., 2000). Glutathione (γ-Glu-Cys-Gly) is the major low-molecular-weight thiol in the cells that controls the cellular thiol/disulfide redox state (Jones, 2002) and serves as a major reservoir for cysteine (Stipanuk, 2004). Reduced glutathione (GSH) is a ubiquitous tripeptide present in greater concentrations in tissue, especially in the intestine (Kelly, 1993; Aw, 1999). Cellular GSH homeostasis is maintained through de novo synthesis from precursor SAA, methionine and cysteine, regeneration from its oxidized form glutathione disulfide, and uptake of extracellular intact GSH via Na+-dependent transport systems (Aw, 1999). Maintaining normal GSH concentration is essential to most tissues, especially the intestine, which is constantly challenged by luminal toxins and oxidants derived from the diet, as well as endogenously generated reactive oxygen species. This has been demonstrated experimentally by inducing marked depletion of GSH with buthionine sulfoximine, resulting in severe degeneration of jejunal and colonic epithelial cells in mice, and this intestinal damage seemed to be prevented by concomitant GSH administration (Märtensson et al., 1990). Moreover, in our recent pig study, we found a marked decrease (about 50%) in glutathione concentration in the small intestine (jejunum and ileum) of piglets fed a SAA-free diet for 7 d compared with a complete diet (Bauchart-Thevret et al., 2009). This finding can be explained by the fact that cysteine is the rate-limiting AA for glutathione synthesis (Lyons et al., 2000; Badaloo et al., 2002; Jackson et al., 2004). Oxidant stress is also known to increase cysteine requirement for cellular glutathione synthesis by activating the transsulfuration pathway (Malmezat et al., 2000b). Cysteine is also a constituent AA of mucins, which are large glycoproteins synthesized by intestinal goblet cells that function in intestinal mucosal innate immune defense (Van Klinken et al., 1997). Thus, because of the rapid turnover of goblet cells and secretion of mucins, the cysteine requirement for their synthesis is likely substantial in the developing intestine.

In conclusion, we demonstrated in vivo in pigs that 40% of dietary cysteine intake is metabolized in splanchnic tissues during first-pass metabolism, of which the GIT uses about 25% of the dietary cysteine intake, representing about 53% of the splanchnic first-pass uptake. In addition, we also found that intestinal absorption was the major metabolic fate of dietary cysteine, representing about 75% intake. Moreover, a substantial proportion of dietary splanchnic cysteine metabolism was consumed by the GIT via nonoxidative pathways. We postulate that glutathione and mucin synthesis are
likely major nonoxidative metabolic fate for cysteine in the gut. Further studies are warranted to determine the nonoxidative metabolic fates for cysteine in the gut.

These studies have implications for dietary methionine needs for gut growth in weanling pigs. Dietary AA are key substrates for intestinal epithelial proliferation and cell function in weanling pigs during the transition from milk of the sow to cereal-based diets. The increased metabolic activity of the intestine consumes a substantial proportion of the dietary intake in the first pass, which can limit the availability of essential nutrients for somatic growth. Cysteine is especially important for the weanling intestine as a precursor for the synthesis of tissue proteins, such as glutathione and goblet cell mucins. Glutathione is especially important because it is a major cellular antioxidant that functions to detoxify intestinal oxidative stress and injury related to microbial-induced inflammation. The results of this study are relevant and underscore the role of the gut on the systemic bioavailability of dietary cysteine in young pigs. The finding that substantial cysteine is metabolized by the gut in the first pass may have implications for dietary methionine needs.

**LITERATURE CITED**


