ASC 684
VFA Metabolism by the Animal

Sources:

Bergman, E. N. 1990. Energy contributions of volatile fatty acids from the gastrointestinal tract in various species. Physiol. Rev. 70: 567-590.

Gäbel, G., and J. R. Aschenbach. 2006. Ruminal SCFA absorption: channeling acids without harm. In: Sejrsen, K., T. Hvelplund, and M.O. Nielsen. Ruminant Physiology. Digestion, Metabolism and Impact of Nutrition on Gene Expression, Immunology and Stress. Wageningen Academic Publishers, Wageningen.

Kristensen, N. B., and D. L. Harmon. 2006. Splanchnic metabolism of short-chain fatty acids in the ruminant. In: Sejrsen, K., T. Hvelplund, and M.O. Nielsen. Ruminant Physiology. Digestion, Metabolism and Impact of Nutrition on Gene Expression, Immunology and Stress. Wageningen Academic Publishers, Wageningen.

Kristensen, N. B., G. B. Huntington, and D. L. Harmon. 2005. Splanchnic carbohydrate and energy metabolism in growing ruminants. In: Burrin, D.G., and H. Mersmann (Eds.) Biology of Metabolism in Growing Animals. Elsevier Limited, London.

I. Importance of VFA to the ruminant
  - A. Estimate about 5 mol VFA/kg DMI (Bergman, 1990)
  - B. Energy substrate
    - 1. VFA account for around 45% of DE intake (Range 20 to 65%)
    - 2. Energy substrate for rumen epithelium
      - a) Butyrate
      - b) LCFA
    - 3. Energy substrate for other tissues (Kidney, Heart, Skelatal Muscle)
      - a) Acetate
      - b) β-OH Butyrate
  - C. Gluconeogenic substrate
      - a) Propionate (non-insulin dependent)
      - b) Lactate
      - c) Other glucogenic precursors include glucogenic amino acids and glycerol
        - (1) Note: primary glucogenic amino acids include glutamate, glutamine, alanine
      - d) Need for glucose
        - (1) Fetal growth
        - (2) Lactation

In some truly exceptional cows whose average milk yield has approached 90 L/d, the requirement for mammary lactose synthesis alone must necessitate a 7-fold increase in glucose production. (Bell and Baumann, 1997. J. Mamm. Gland Biol. and Neoplasia. 2:265).

        - (3) Brain & nerve tissues

(4) Maintenance of blood glucose levels (though lower than in nonruminants)

e) Importance of gluconeogenesis in ruminants

(1) As little at 10% of the required glucose comes from glucose absorbed from the digestive tract (90% must be synthesized) – (Young, 1977)

(a) High extreme – heavily lactating dairy cow, could amount to ~ 7 kg glucose/day

(b) Lower end – 200 kg steers just above maintenance ~.6 kg glucose/day

D. Lipogenic substrate

a) Acetate

b) β-OH Butyrate

II. Absorption of VFA

A. About 2/3 to ¾ disappear in the rumen

1. Absorption by ruminal epithelium

a) Most metabolic activity in ruminal epithelium is in basal cells (high mitochondrial concentration)

b) Passive transport

(1) Decreasing pH →Increasing absorption

(2) SCFA have high permeability across biological membranes compared with LCFA

c) Challenge to importance of passive transport

(1) Absorption of acetate and propionate not directly proportional to concentration of protonized acid

d) Importance of active transport controversial

(1) Russell and Gahr – active transport is predominant form

(2) Kristensen et al. – "So far, the data available on SCFA absorption from the forestomach seem to indicate that absorption of SCFA by diffusion can account for the quantitatively most important SCFA absorption."

2. Intraruminal interconversions

B. Remainder (1/4 to 1/3) pass through R/O orifice

1. Most absorbed in omasum and abomasum (very little makes it to the SI)

C. Hindgut SCFA absorption

1. 6 to 13% of total gut absorption

III. Postabsorptive Fate

A. Epithelial metabolism

1. Bergman and Wolff (1971) – simultaneous measurement of VFA production (isotope infusion) and portal VFA absorption.

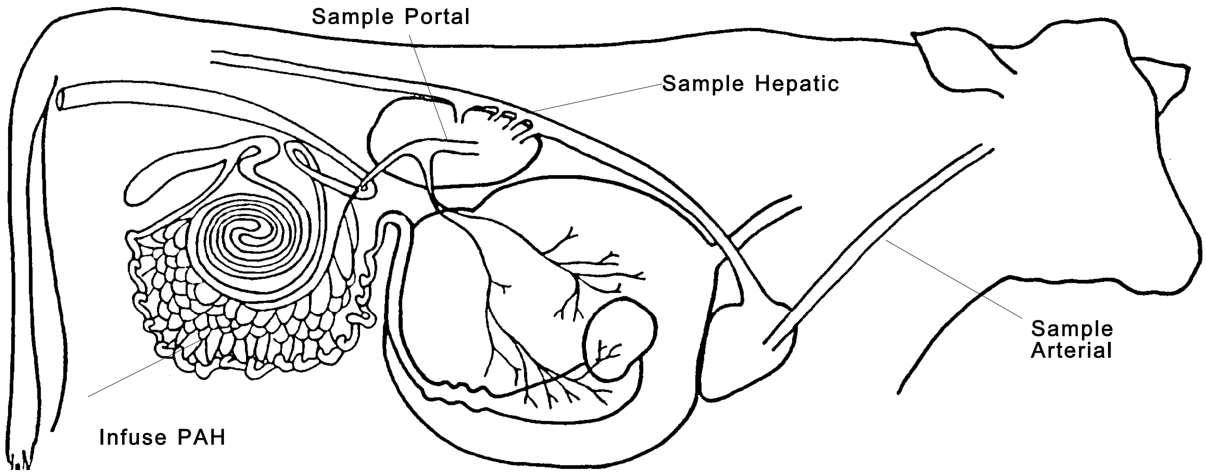

TABLE 2. *Comparison of rumen production of VFA with portal absorption and rumen epithelial metabolism*

	Volatile Fatty Acids			
	Acetic	Propionic	Butyric	Reference
Sheep fed hay				
Rumen production, mol/day*	3.3	0.9	0.6	51, 191
Portal absorption, mol/day	2.3	0.44	0.05	52, 53
Difference, %	30	50	90	
In vitro rumen epithelium†				
Metabolism, %	45	65	85	277

* Measured by isotope dilution in rumen. † Amounts metabolized by isolated sheets of rumen epithelium as a percentage of that removed from medium.

2. Problem – difficult to justify quantitatively
   a) Rumen epithelium of lactating cow would have oxidative needs comparable to the entire fasting heat metabolism of the cow (Kristensen and Danfaer, 2001)
3. More recent work – Kristensen and Harmon, 2006:

Table 1. Portal vein recovery (%) of SCFA infused into a functional rumen of sheep or into the washed rumen of sheep or steers.

	Functional rumen	Washed rumen	
Item	**Sheep**	**Sheep**	**Steer**
Acetate[1]	54 ± 8[2]	109 ± 7[4]	105 ± 3[5]
Propionate	62 ± 7[2]	95 ± 7[4]	91 ± 2[5]
Isobutyrate	60 ± 3[3]	102 ± 9[4]	101 ± 9[6]
Butyrate	11 - 25 ± 2[2]	23 ± 3[4]	18 - 52 ± 4[6]
Isovalerate	-	48 ± 5[4]	54 ± 4[5]
Valerate	14 - 31 ± 2[3]	32 ± 4[4]	16 - 54 ± 3[6]
Caproate	-	-	54 ± 2[7]
Heptanoate	-	-	43 ± 2[7]

[1]Values for acetate are corrected for PDV uptake of arterial acetate using systemic infusion of [2-[13]C]acetate.

[2](Kristensen *et al.*, 1996), [3](Kristensen *et al.*, 2000b), [4](Kristensen *et al.*, 2000a), [5](Kristensen and Harmon, 2004c), [6](Kristensen and Harmon, 2004a), [7](Kristensen and Harmon, 2004b)

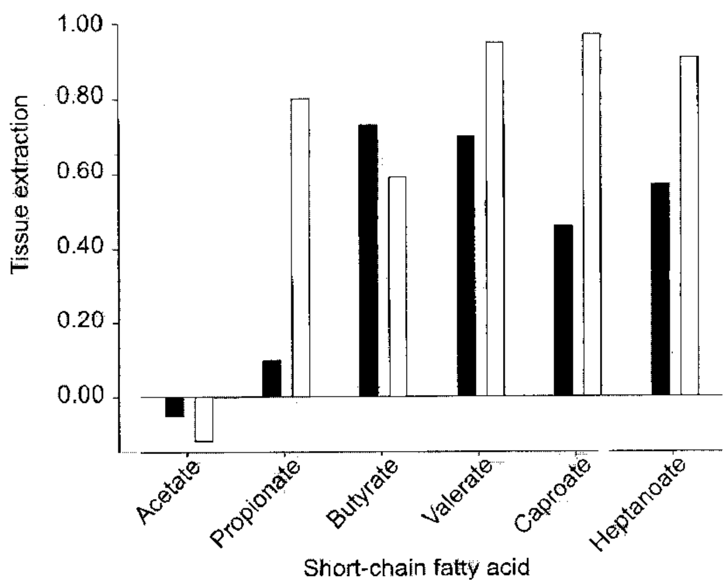

Figure 1. Fractional extraction of short-chain fatty acids in ruminal epithelium (closed bar) and liver (open bar). Data from washed rumen experiments with steers (Kristensen and Harmon, 2004c; Kristensen and Harmon, 2004a; Kristensen andHarmon, 2004b).

4. Butyrate is the primary fuel for the ruminal epithelium
5. Postruminal GI tissues do metabolize significant quantities of acetate

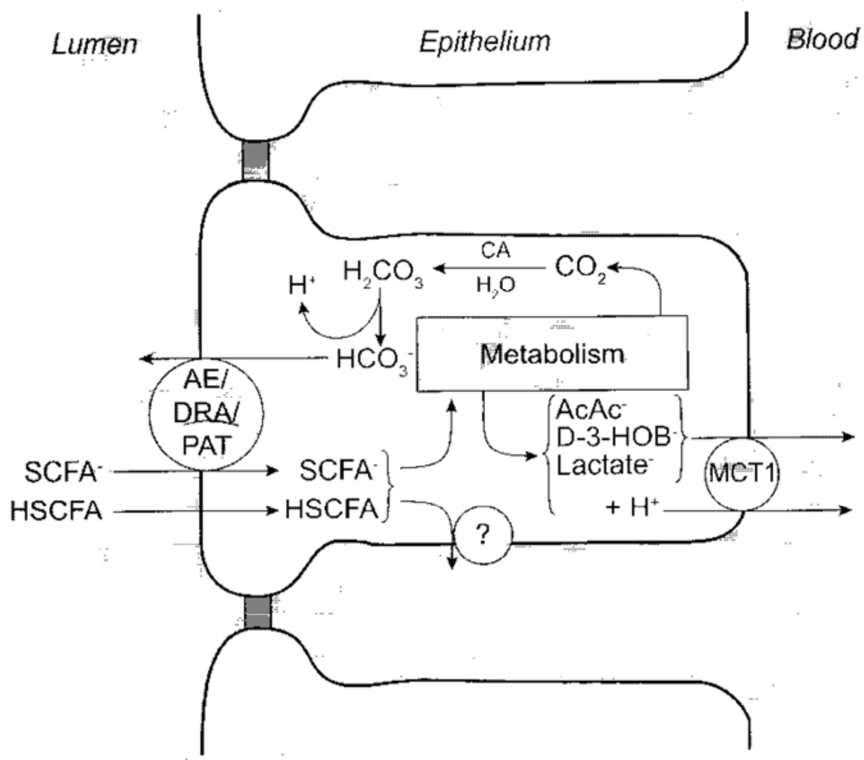

Figure 1. Transport of SCFA across ruminal epithelium.

Apical uptake of SCFA surely occurs via diffusion of undissociated SCFA (HSCFA). Additional absorption of dissociated SCFA (SCFA-) by anion exchange proteins (AE, DRA, or PAT) is suggested by functional studies in vivo and in vitro (Ash and Dobson, 1963; Gäbel et al., *1991b; Kramer* et al., *1996; Sehested* et al., *1999a,b) and by molecular biological studies. After uptake, SCFA are partially metabolized through oxidative or anaerobic pathways. Carbon dioxide from the oxidative breakdown can be further transformed by the activity of carboanhydrase (CA) to H_2CO_3 which in turn dissociates into HCO_3^- and H^+. HCO_3^- may drive the apical anion exchangers. Fate of H^+ is outlined in Figure 2. Ketone bodies (AcAc-, acetoacetate; D-3-HOB-, D-3-hydroxybutyrate) and lactate derived from the anaerobic breakdown can be extruded on the basolateral side by the proton-linked monocarboxylate transporter MCT1. Basolateral extrusion of SCFA partly takes places by simple diffusion of HSCFA. If and which anion exchange proteins or other transport proteins are involved has to be elucidated.*

Besides MCT1, the localisation of transport proteins is so far only derived from functional studies and from comparisons with other gastrointestinal epithelia. MCT1 has been localized by immunocytochemical methods (Figure 6). The multilayered structure of the rumen epithelium is reduced to one layer in the model presented. Consequently, the "basolateral membrane" represents the blood oriented side of the cells in the stratum basale. The "apical membrane" is located on the lumen oriented side of the cells in the upper layers of the epithelium