Effects of Metabolites on Feed Intake in Dairy Cows

M. S. Allen and B. J. Bradford, Michigan State University

Effects of Endproducts of Ruminal Fermentation on Energy Intake and Partitioning in Ruminants

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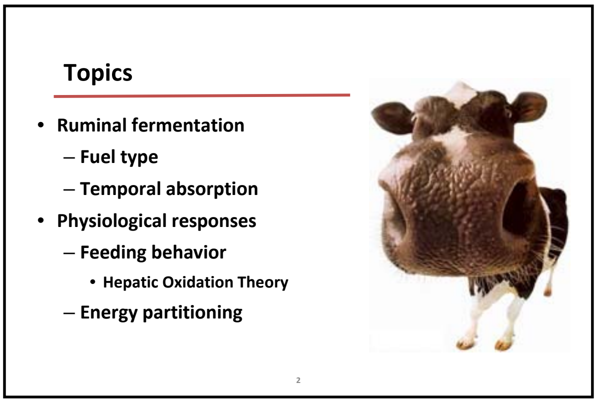
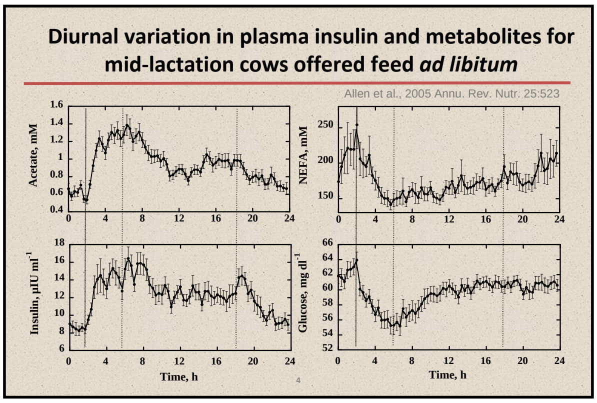


Topics

- Ruminal fermentation
  - Fuel type
  - Temporal absorption
- Physiological responses
  - Feeding behavior
    - Hepatic Oxidation Theory
  - Energy partitioning

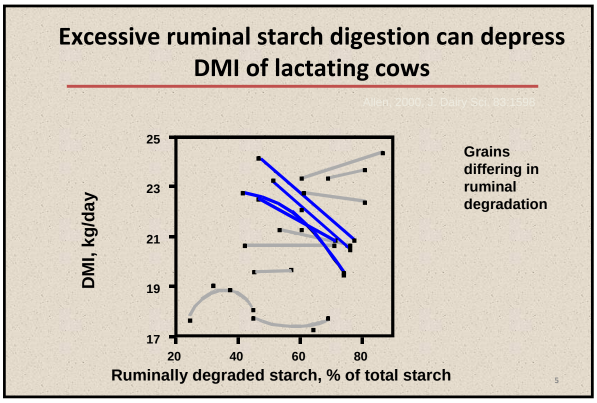
Absorbed fuels

- Vary by type and temporal absorption
- Highly affected by concentration and fermentability of starch in diet.
- Fuels affected by ruminal fermentation
  - Short-chain fatty acids
  - Glucose (starch escaping rumen)
  - Lactate (intestinal metabolism of starch)
  - Amino acids (feed degradation, microbial production)
  - Long-chain fatty acids (biohydrogenation)



Diurnal variation in plasma insulin and metabolites for mid-lactation cows offered feed *ad libitum*

Allen et al., 2005 Annu. Rev. Nutr. 25:523



Excessive ruminal starch digestion can depress DMI of lactating cows

Allen, 2000, J. Dairy Sci. 83:1598

Feed Intake

***f* (meal size, intermeal interval)**

↑ ↑

satiety **hunger**

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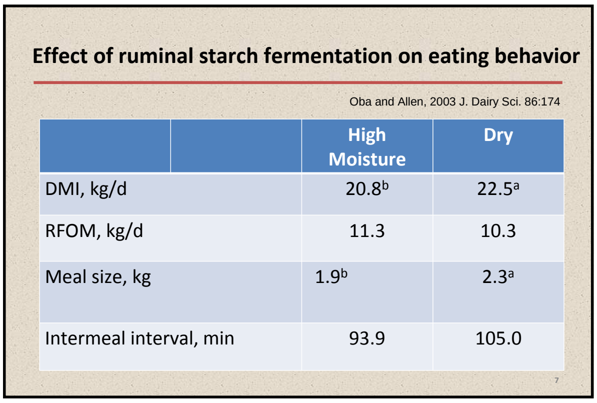
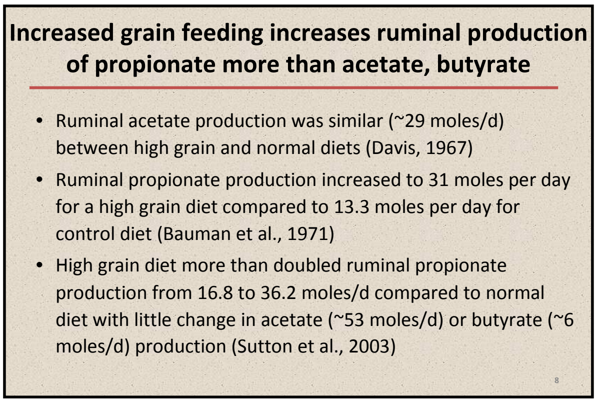


Effect of ruminal starch fermentation on eating behavior

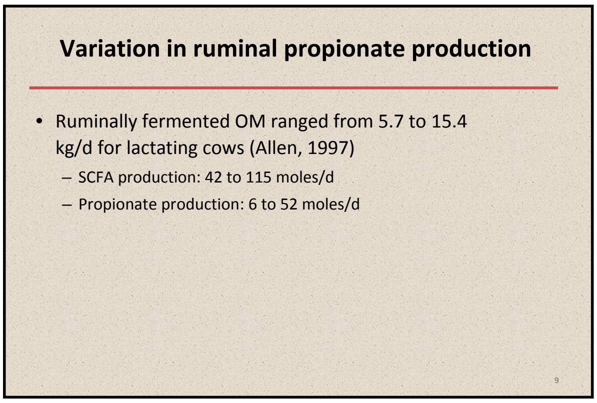
Oba and Allen, 2003 J. Dairy Sci. 86:174

		High Moisture	Dry
DMI, kg/d		20.8^b	22.5^a
RFOM, kg/d		11.3	10.3
Meal size, kg		1.9^b	2.3^a
Intermeal interval, min		93.9	105.0



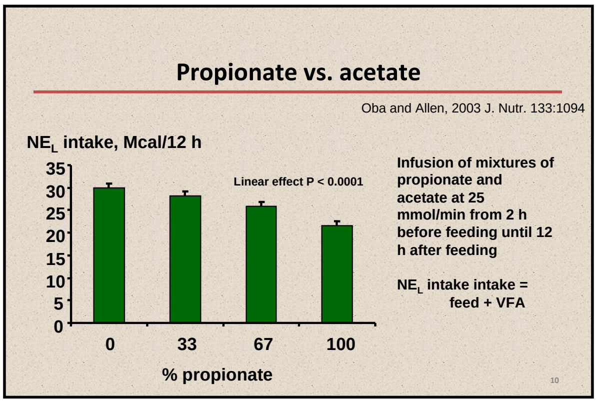
Increased grain feeding increases ruminal production of propionate more than acetate, butyrate

- Ruminal acetate production was similar (~29 moles/d) between high grain and normal diets (Davis, 1967)
- Ruminal propionate production increased to 31 moles per day for a high grain diet compared to 13.3 moles per day for control diet (Bauman et al., 1971)
- High grain diet more than doubled ruminal propionate production from 16.8 to 36.2 moles/d compared to normal diet with little change in acetate (~53 moles/d) or butyrate (~6 moles/d) production (Sutton et al., 2003)



Variation in ruminal propionate production

- Ruminally fermented OM ranged from 5.7 to 15.4 kg/d for lactating cows (Allen, 1997)
  - SCFA production: 42 to 115 moles/d
  - Propionate production: 6 to 52 moles/d

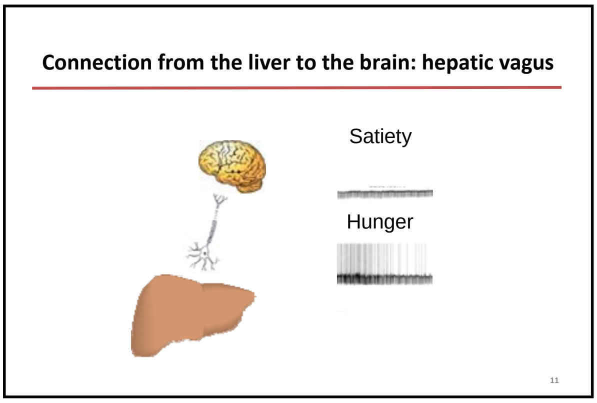


Propionate vs. acetate

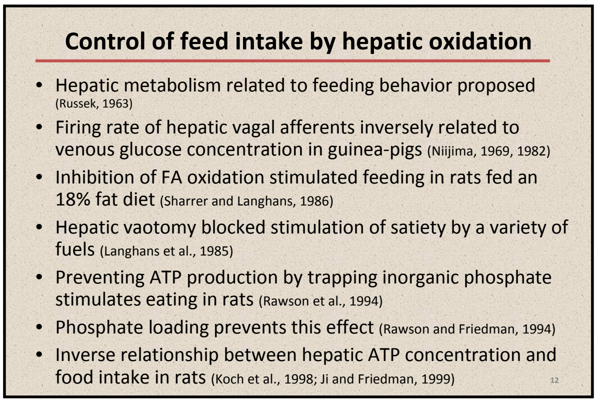
Oba and Allen, 2003 J. Nutr. 133:1094

Infusion of mixtures of propionate and acetate at 25 mmol/min from 2 h before feeding until 12 h after feeding

NE_L intake intake = feed + VFA



Connection from the liver to the brain: hepatic vagus



Control of feed intake by hepatic oxidation

- Hepatic metabolism related to feeding behavior proposed (Russek, 1963)
- Firing rate of hepatic vagal afferents inversely related to venous glucose concentration in guinea-pigs (Niijima, 1969, 1982)
- Inhibition of FA oxidation stimulated feeding in rats fed an 18% fat diet (Sharrer and Langhans, 1986)
- Hepatic vaotomy blocked stimulation of satiety by a variety of fuels (Langhans et al., 1985)
- Preventing ATP production by trapping inorganic phosphate stimulates eating in rats (Rawson et al., 1994)
- Phosphate loading prevents this effect (Rawson and Friedman, 1994)
- Inverse relationship between hepatic ATP concentration and food intake in rats (Koch et al., 1998; Ji and Friedman, 1999)

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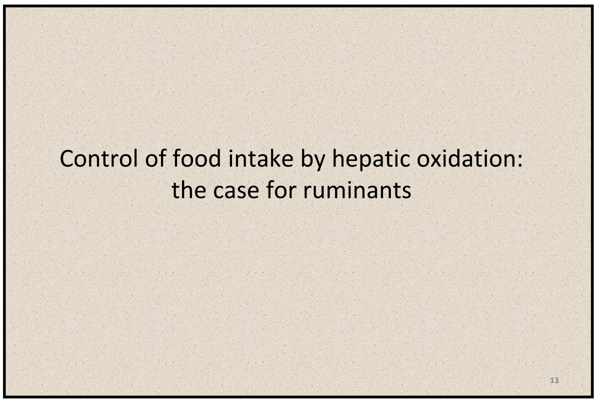
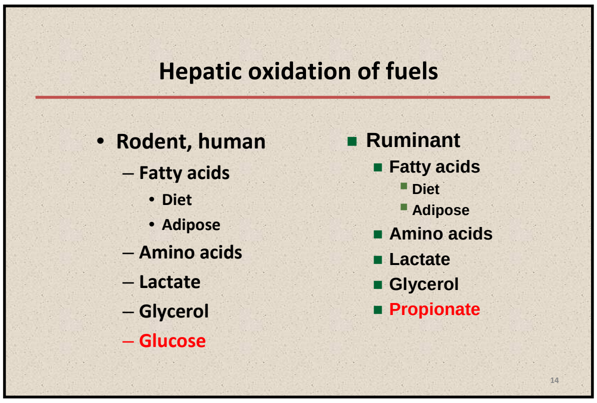


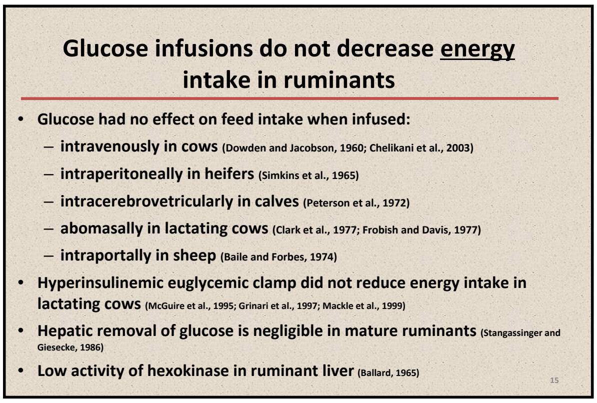
Control of food intake by hepatic oxidation:
the case for ruminants



Hepatic oxidation of fuels

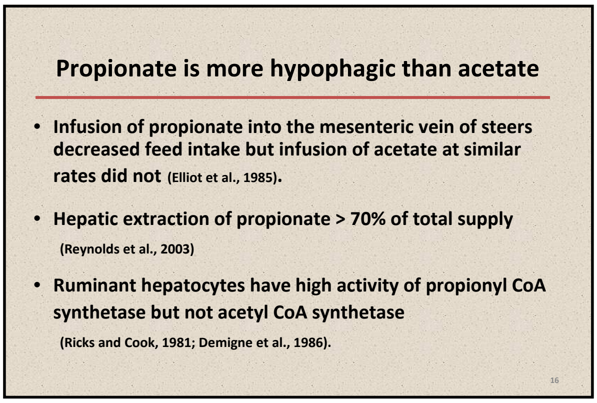
- **Rodent, human**
  - **Fatty acids**
    - **Diet**
    - **Adipose**
  - **Amino acids**
  - **Lactate**
  - **Glycerol**
  - **Glucose**

- **Ruminant**
  - **Fatty acids**
    - **Diet**
    - **Adipose**
  - **Amino acids**
  - **Lactate**
  - **Glycerol**
  - **Propionate**



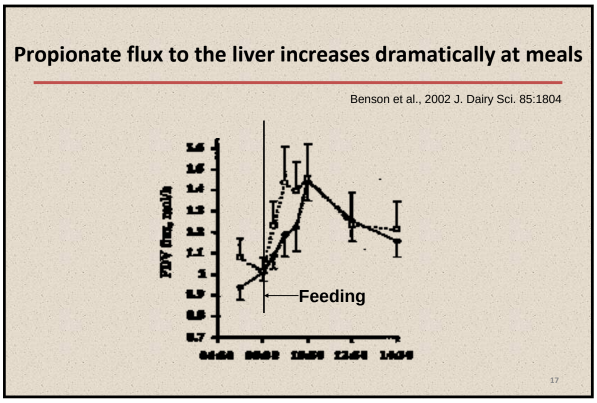
Glucose infusions do not decrease energy intake in ruminants

- **Glucose had no effect on feed intake when infused:**
  - **intravenously in cows** (Dowden and Jacobson, 1960; Chelikani et al., 2003)
  - **intraperitoneally in heifers** (Simkins et al., 1965)
  - **intracerebrovetricularly in calves** (Peterson et al., 1972)
  - **abomasally in lactating cows** (Clark et al., 1977; Frobish and Davis, 1977)
  - **intraportally in sheep** (Baile and Forbes, 1974)
- **Hyperinsulinemic euglycemic clamp did not reduce energy intake in lactating cows** (McGuire et al., 1995; Grinari et al., 1997; Mackle et al., 1999)
- **Hepatic removal of glucose is negligible in mature ruminants** (Stangassinger and Giesecke, 1986)
- **Low activity of hexokinase in ruminant liver** (Ballard, 1965)



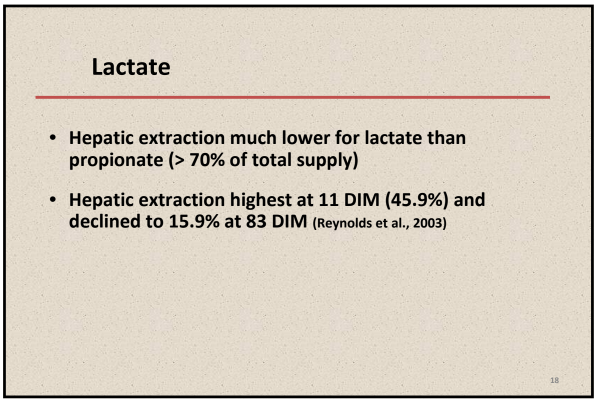
Propionate is more hypophagic than acetate

- **Infusion of propionate into the mesenteric vein of steers decreased feed intake but infusion of acetate at similar rates did not** (Elliot et al., 1985).
- **Hepatic extraction of propionate > 70% of total supply**
  (Reynolds et al., 2003)
- **Ruminant hepatocytes have high activity of propionyl CoA synthetase but not acetyl CoA synthetase**
  (Ricks and Cook, 1981; Demigne et al., 1986).



Propionate flux to the liver increases dramatically at meals

Benson et al., 2002 J. Dairy Sci. 85:1804



Lactate

- **Hepatic extraction much lower for lactate than propionate (> 70% of total supply)**
- **Hepatic extraction highest at 11 DIM (45.9%) and declined to 15.9% at 83 DIM** (Reynolds et al., 2003)

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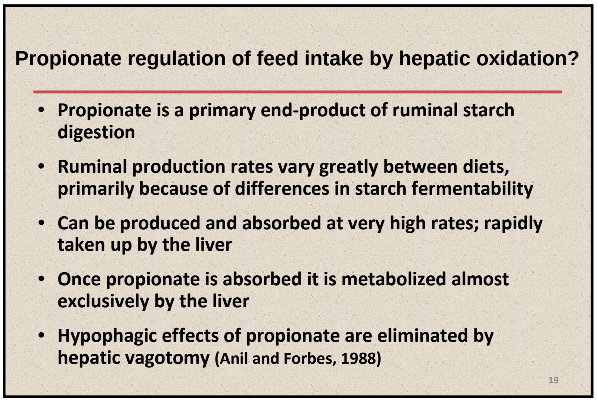
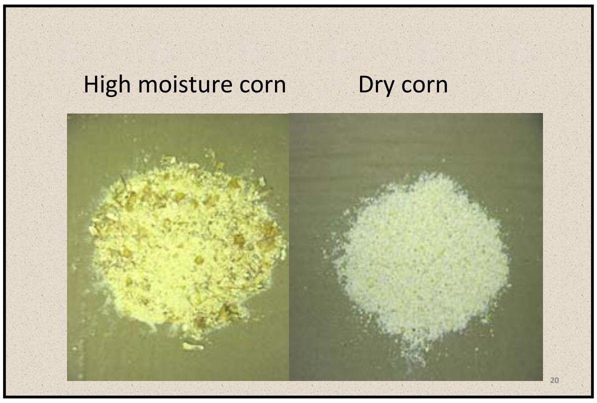
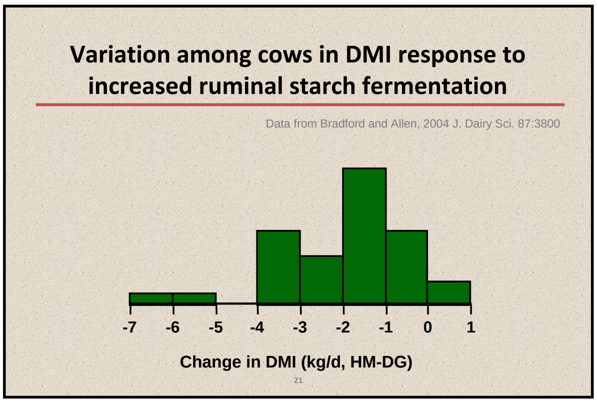


Propionate regulation of feed intake by hepatic oxidation?

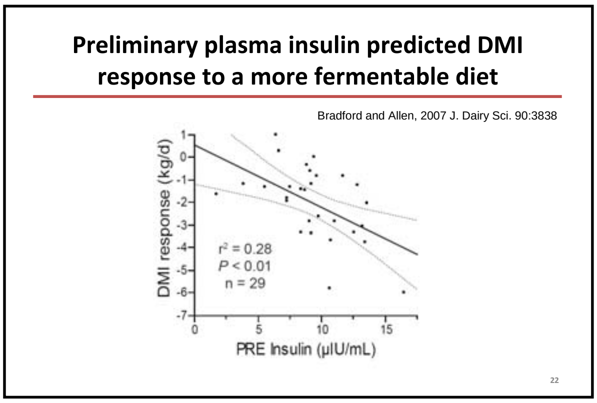
- Propionate is a primary end-product of ruminal starch digestion
- Ruminal production rates vary greatly between diets, primarily because of differences in starch fermentability
- Can be produced and absorbed at very high rates; rapidly taken up by the liver
- Once propionate is absorbed it is metabolized almost exclusively by the liver
- Hypophagic effects of propionate are eliminated by hepatic vagotomy (Anil and Forbes, 1988)





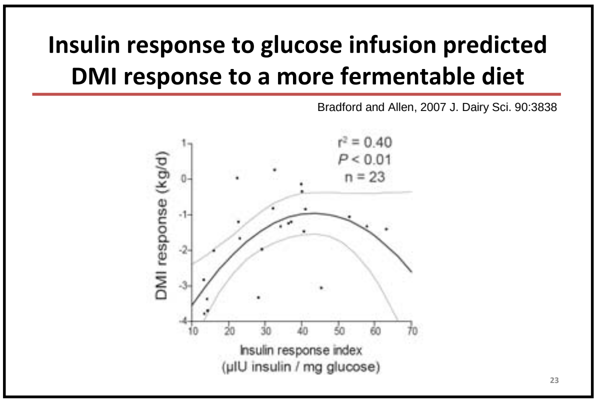
Variation among cows in DMI response to increased ruminal starch fermentation

Data from Bradford and Allen, 2004 J. Dairy Sci. 87:3800



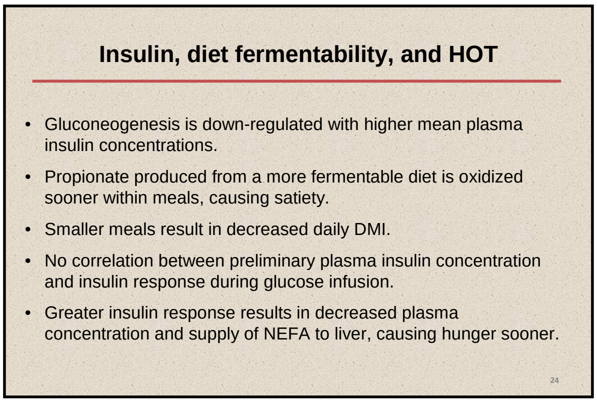
Preliminary plasma insulin predicted DMI response to a more fermentable diet

Bradford and Allen, 2007 J. Dairy Sci. 90:3838



Insulin response to glucose infusion predicted DMI response to a more fermentable diet

Bradford and Allen, 2007 J. Dairy Sci. 90:3838



Insulin, diet fermentability, and HOT

- Gluconeogenesis is down-regulated with higher mean plasma insulin concentrations.
- Propionate produced from a more fermentable diet is oxidized sooner within meals, causing satiety.
- Smaller meals result in decreased daily DMI.
- No correlation between preliminary plasma insulin concentration and insulin response during glucose infusion.
- Greater insulin response results in decreased plasma concentration and supply of NEFA to liver, causing hunger sooner.

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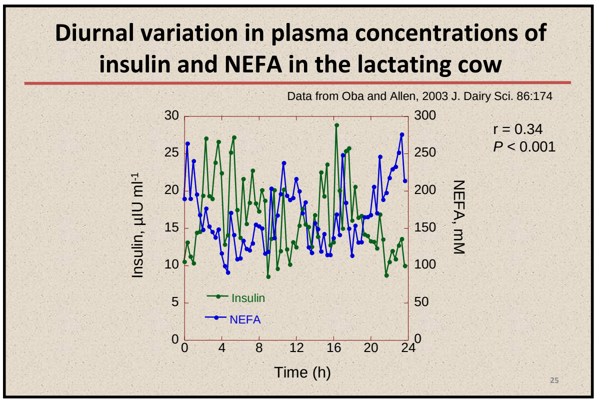
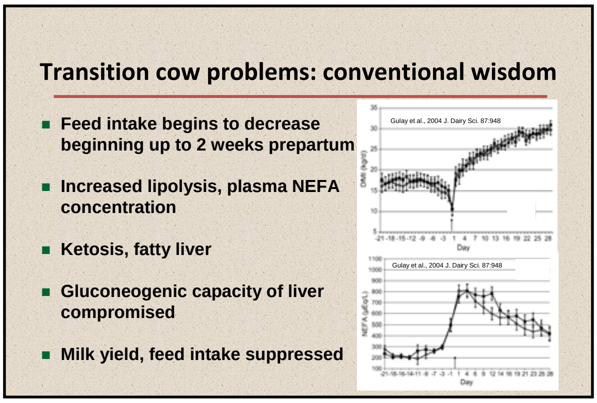


Diurnal variation in plasma concentrations of insulin and NEFA in the lactating cow

Data from Oba and Allen, 2003 J. Dairy Sci. 86:174

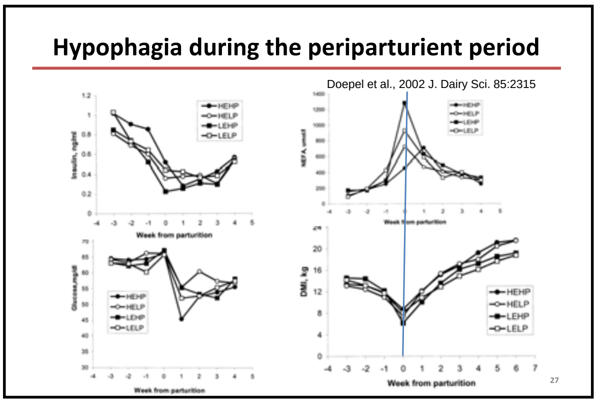


Transition cow problems: conventional wisdom

- Feed intake begins to decrease beginning up to 2 weeks prepartum
- Increased lipolysis, plasma NEFA concentration
- Ketosis, fatty liver
- Gluconeogenic capacity of liver compromised
- Milk yield, feed intake suppressed

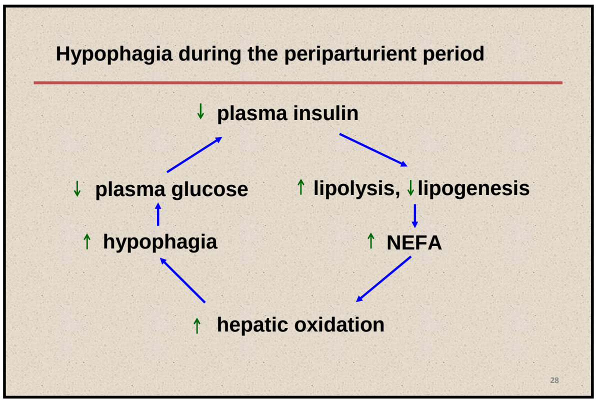
Gulay et al., 2004 J. Dairy Sci. 87:948

Gulay et al., 2004 J. Dairy Sci. 87:948



Hypophagia during the periparturient period

Doepel et al., 2002 J. Dairy Sci. 85:2315



Hypophagia during the periparturient period

↓ plasma insulin

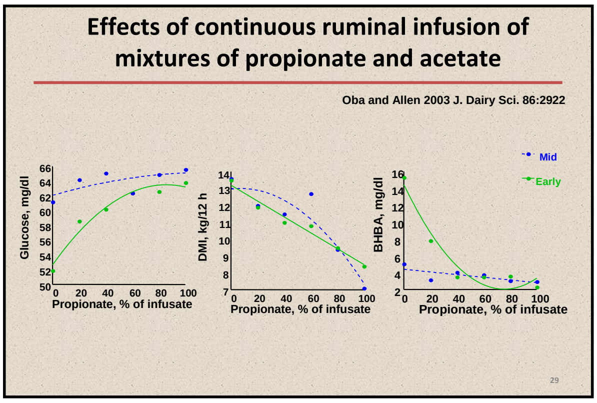
↓ plasma glucose

↑ lipolysis, ↓lipogenesis

↑ hypophagia

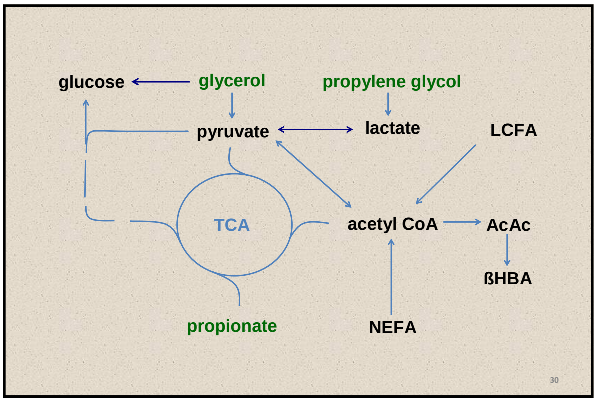
↑ NEFA

↑ hepatic oxidation



Effects of continuous ruminal infusion of mixtures of propionate and acetate

Oba and Allen 2003 J. Dairy Sci. 86:2922



glucose

glycerol

propylene glycol

pyruvate

lactate

LCFA

TCA

acetyl CoA

AcAc

ßHBA

propionate

NEFA

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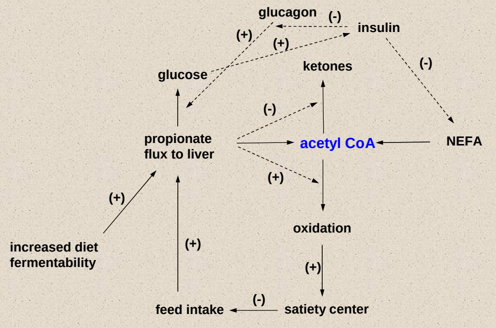
Model by which propionate may stimulate satiety



HOT is consistent with:

- Hypophagic effects of propionate compared to acetate
- Effects of hepatic vagotomy on hypophagia from propionate
- Hypophagic effects of glucose: ruminants vs. non-ruminants
- Variable effects of increased ruminal starch fermentation on feed intake
- Hypophagia during the periparturient period
- Effects of insulin and glucagon on feed intake
- Efficacy of ketosis treatments

Effects of Ruminal Fermentation on Energy Partitioning

Effect of bm3 corn silage on intake and production of dairy cows fed low or high NDF diets

Oba and Allen, 2000, J. Dairy Sci. 83:1333

	29% NDF		38% NDF		Significance, *P*		
	bm3	control	bm3	control	NDF	CS	NDFxC
Corn grain, % DM	26	29	0	5			
DMI, kg/d	24.7	23.9	22.9	21.5	<0.001	0.02	NS
3.5% FCM, kg/d	35.6	34.3	35.8	32.6	NS	0.06	NS
BW gain, kg/d	1.10	0.79	0.00	-0.02	< 0.01	NS	NS

Substitution of beet pulp for barley grain in late lactation

Mahjoubi et al., 2009, AFST 153:60-66

18 Holstein cows
last 2 months of lactation
171±16 days pregnant
289±35 DIM
Treatments:
0 BP, 23.5% BG
(19.0% starch)
8.6% BP, 14.9% BG
(15.1% starch)
17.2% BP, 6.3% BG
(12.3% starch)

	0%	8.6%	17%	*P*
DMI, kg/d	18.1	17.5	17.7	NS
Milk, kg/d	17.9	17.4	17.9	NS
Milk fat, kg/d	0.78	0.84	0.90	0.1, L
MEO, MJ/d	58.2	60.0	63.5	0.1, L
BCS, units/per.	+0.13	-0.09	-0.12	0.01, L
BFT, mm/per.	+2.5	-0.4	-1.6	<0.01,L
Insulin, ng/ml	0.93	0.75	0.72	0.05, L
pH	5.77	5.96	6.21	0.001, L

Effect of fat source on energy partitioning

Harvatine and Allen, 2006 J. Dairy

8 Holstein cows in early lactation (77 DIM)
Control diet (CON; 5.5% FA)
2.5% supplemental FA:
SAT: Energy Booster 100®
UNS: Megalac R®
Int: 50:50 mix

	Con	Sat	Int	Uns
DMI, lb/d	60.6	56.5	55.2	53.0
DE intake, Mcal/d	78.0	75.3	74.0	70.1
Milk, lb/d	103.4	102.5	99.4	96.1
Milk fat, lb/d	3.19	3.01	2.77	2.42
18:1 *trans* duod. flow, g/d	158	167	276	264
t10, c12 CLA g/100g of milk FA	0.02	0.03	0.04	0.08
BW gain, lb/d	0.46	0.24	1.08	2.07

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CLA and energy partitioning

Harvatine et al., J. Nutr. 139: 849–854, 2009

- Infusion of trans 10, cis 12 CLA: decreased milk fat yield 38%
- Increased adipose tissue expression of lipid synthesis enzymes (lipoprotein lipase, FA synthase, stearoyl-CoA desaturase, and FA binding protein 4)
- Increased regulators of lipid synthesis (sterol-response element binding protein 1, thyroid hormone responsive spot 14, and PPARg)
- “Results are consistent with energy spared from the reduction in milk fat synthesis being partitioned toward adipose tissue fat stores during short-term MFD.”

Conclusion

Ruminal fermenation alters the type and temporal absorption of fuels available for intermediary metabolism, greatly affecting energy intake and partitioning.

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