A Discussion of Essential vs Required Nutrients – Mostly AA

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Overview

- What are essential nutrients vs required nutrients?
- Implications for both energy and protein requirements
- Examples of essential and required nutrients and metabolism
- Where the interaction might limit productivity
- Summary

Essential vs Required Nutrients

- An essential nutrient is a substance required by the body for survival, growth, and reproduction that allow for essential functions.
- Essential nutrients cannot be made endogenously but can be interconverted to other forms of nutrients
- “Essential amino acids” such as: Methionine, lysine, histidine, etc
- Carbohydrates
- Energy
- Minerals
- Vitamins

Required nutrients

- What’s the difference between required vs essential?
- Required can be made from other metabolites, synthesized or interconverted
- An easy example is non-essential amino acids

Metabolizable Protein

- Sum of essential amino acids and non-essential amino acids
- We account for essential AA (EAA) and assume the non-essential AA are met by metabolism as they make up the balance of the MP-EAA
- Cattle consume NEAA similarly to EAA
- The NEAA "generally" make up between 46% - 53% of total AA intake
- Thus, intake of NEAA and rumen escape will provide MP as NEAA just like EAA
- And of course, microbial protein is also comprised of both EAA and NEAA

Non-essential Amino Acids

- Can be made by various pathways using EAA and other substrates
- Synthesis is energy intensive
- Can possibly be limiting under conditions of high demand
- Implies a reduced efficiency of use of EAA if converted to NEAA as not use directly for protein metabolism

Nutrient signaling and metabolic flexibility in the mammary gland: Key to improved NUE?

Mammary gland is one of the most adaptable organs in mammals

- Main sources of nutrient uptake for intermediary metabolism: acetate, glucose, ketones, and AA
- Ability to manipulate blood flow according to lactation requirements and in recognition of varying nutrient supply
- Uptake to output ratio of AA in mammary gland is not uniform across AA and changes in response to profile and supply of AA observed in circulation → Group 1, 2, and 3 AA

Milk protein synthesis requires activation/repression of key metabolic pathways

- mTORC1 and AMPk pathways
  - Activated through hormone signaling (insulin, IGF-1), intracellular nutrients (AA supply; Leucine), and energy status (ATP:AMP ratio)
- Integrated stress response (ISR) pathway
  - Reduces cellular anabolic load in the presence of intracellular stress
  - Indirectly inhibited by insulin and IGF-1 and ATP status
- Unfolded protein response (UPR) pathway
  - Restores endoplasmic reticulum homeostasis through multiple cellular responses
  - Initiation causes direct phosphorylation of PERK → activation of ISR pathway

Optimal supply of AA with improved energy status → Maximized anabolic output

Mammary adaptability in varying nutrient supplies

Shifts in nutrient profile and supply → alterations in their efficient use according to mammary demand.

Extraction of BCAA changes across lactation

- Cellular maintenance and anabolic response (Mepham, 1982)

Lysine undergoes obligate catabolism in mammary (Lapierre, 2009)

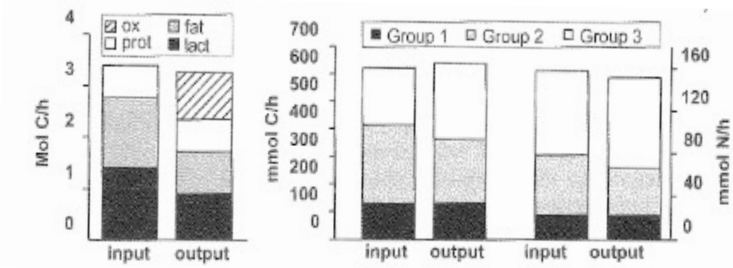
- Supplies N for NEAA synthesis
- Level of catabolism can shift in accordance with NEAA supply

Arginine is taken up in drastic excessive relative to milk protein output (~2.5x)

- Catabolism products include proline, ornithine, and urea (O'Quinn et al., 2002)
- Proline content in milk casein = 10.4% (2nd highest to glutamine)

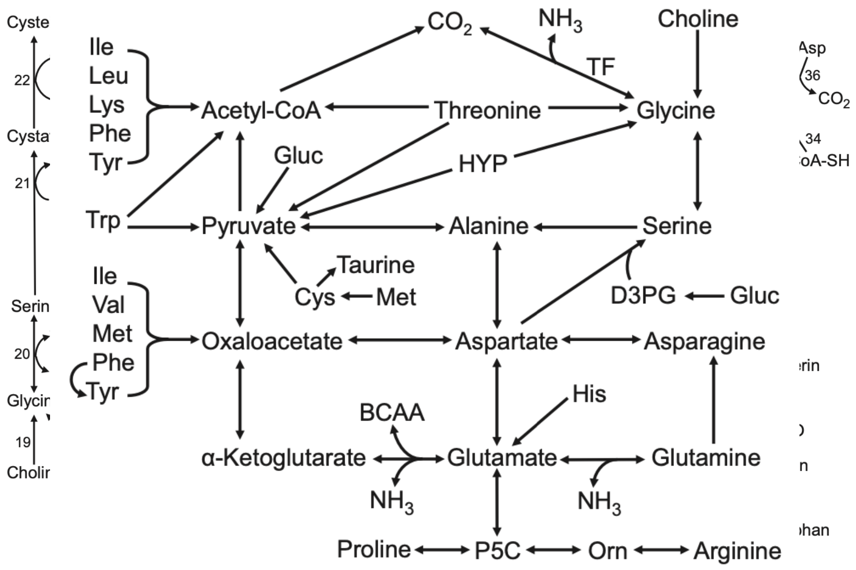
	AA Group (Mepham, 1982)		
	1	2	3
Amino Acid	Histidine	Isoleucine	Alanine
	Phenylalanine	Leucine	Asparagine
	Methionine	Valine	Cysteine
	Tyrosine	Lysine	Glutamine
	Tryptophan	Arginine*	Glycine
		Threonine*	Proline
			Serine
Efficiency (AA –N uptake/AA-N Milk)	1	> 1.15	< 1

* Suggested group according to Lapierre et al. (2012)



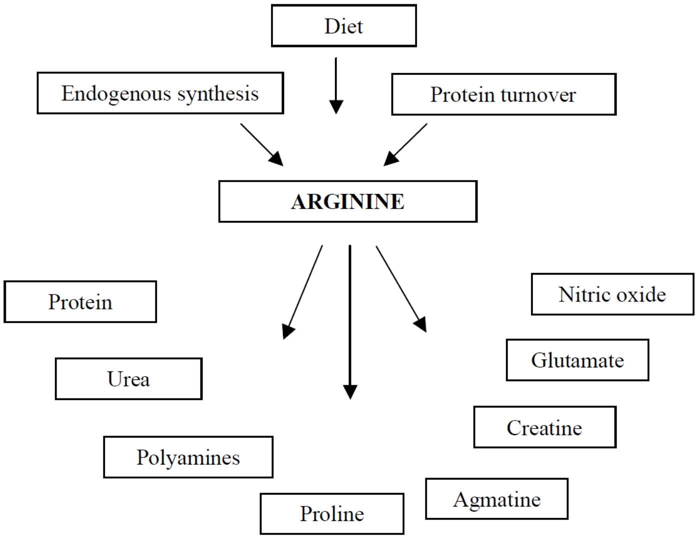
Adapted from Lobley (2007) based on data from Lemosquet (2009) and Raggio (2006)

“Non-Essential” Amino Acids



Wu 2022

Sources and metabolic products of arginine.
Adapted from (Morris, 2006).



Lapierre et al. 2012

Mammary Arg uptake to output 2:45:1

Range 0.88 to 4.18

47 observations

Effect of Increasing Rumensin Concentration on the Performance of Lactating Dairy Cows Fed Contemporary Diets

Objectives

1. Redefine the effects of monensin fed at four levels on milk production efficiency of dairy cows fed modern diets
2. Evaluate the relationship between monensin dose and milk fat production in dairy cows fed modern diets
3. Characterize the impact of various doses of monensin on milk fatty acid profile using modern high-throughput technology

It is important to recognize that at treatment assignment, the cows were producing 90-92 lb milk, 3.9% fat and 3.1% true protein

Ingredient Composition of Experimental Diets

	Diet[1]				
Ingredient, % of DM	Covariate	CON	R11	R14.5	R18
Corn silage	34.9	34.9	34.9	34.9	34.9
Grass haylage	19.4	19.4	19.4	19.4	19.4
Corn, ground fine	18.0	18.0	18.0	18.0	18.0
Soybean meal	6.81	6.81	6.81	6.81	6.81
SoyPass[2]	5.83	5.83	5.83	5.83	5.83
Citrus pulp	4.49	4.49	4.49	4.49	4.49
Wheat middlings	4.49	4.49	4.49	4.49	4.49
Dextrose	1.60	1.60	1.60	1.60	1.60
Bloodmeal	1.00	1.00	1.00	1.00	1.00
Bergafat F100[3]	0.60	0.60	0.60	0.60	0.60
Energy booster 100[4]	0.60	0.60	0.60	0.60	0.60
Limestone, ground	0.56	0.56	0.56	0.56	0.56
Vitamins and minerals	1.35	1.35	1.35	1.35	1.35
Magnesium oxide	0.11	0.11	0.11	0.11	0.11
Smartamine M[7]	0.10	0.10	0.10	0.10	0.10
Smartamine ML[8]	0.10	0.10	0.10	0.10	0.10
Levucell SC[9]	0.05	0.05	0.05	0.05	0.05
Rumensin 90[10]	0.006	----	0.006	0.008	0.01

Diet formulation characteristics

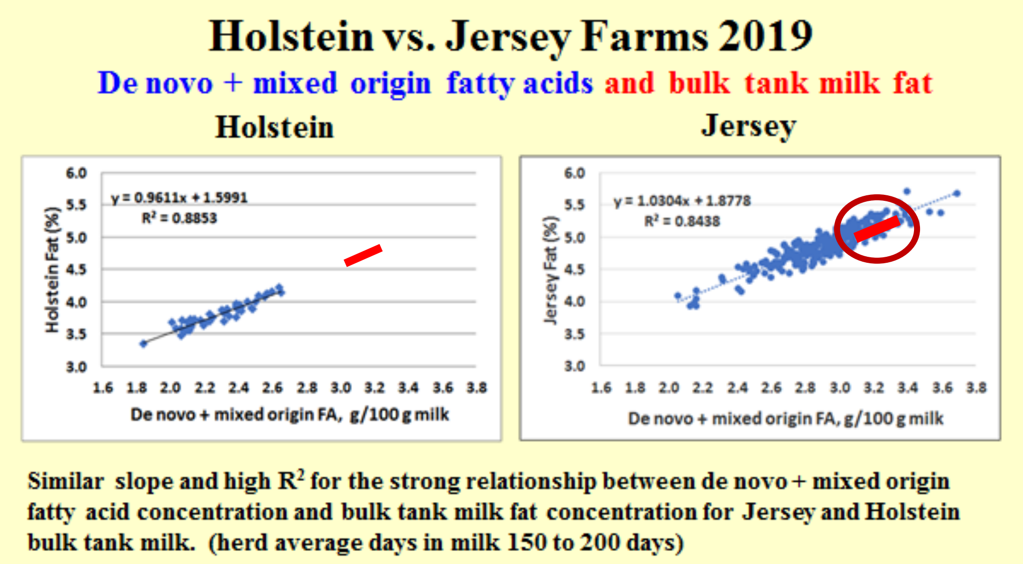
- 54% forage diet – formulated to achieve the lowest uNDF for the highest aNDFom digestible pool for the available forages
- Dry ground corn from the farm – moderate starch
- Sugar added to enhance rumen fermentation, increase microbial flow (bacteria and protozoa) and fiber digestion - older data from Hoover indicating that 5-7% sugar in TMR diets is beneficial for component yields
- Rumen protected methionine and lysine formulated at levels reflecting our new requirement data – 1.19 grams methionine/Mcal ME and lysine set at 2.7 times the methionine – these values are many grams higher than previously fed
- Utilized a blend of fatty acids, higher in Palmitic (0.432 lb), Stearic (0.144 lb) and Oleic (0.02 lb) – moderate in RUFAL – in previous research achieving 1.5:1 palmitic:oleic enhanced milk protein synthesis likely through insulin signaling

Effect of increasing dietary monensin concentration on lactation performance

	Diet[1]					P-value[2]			
Item	CON	R11	R14.5	R18	SEM	Linear	Quad	Trt	Trt x Wk
Days in milk[3]	190	168	193	184	7.2	-	-	-	-
Monensin, mg/d	0	384	465	589	-	-	-	-	-
DMI, kg/d	26.9	26.8	26.7	27.7	0.31	0.29	0.09	0.22	< 0.01
Milk, kg/d	39.3	39.9	39.7	39.6	0.34	0.48	0.38	0.69	< 0.01
Fat, %	**4.60**	**4.67**	**4.71**	**4.66**	0.04	0.16	0.40	0.38	0.16
Fat, kg/d	1.79	1.83	1.85	1.83	0.02	0.15	0.52	0.40	< 0.01
Protein, %	**3.35**	**3.37**	**3.36**	**3.39**	0.02	0.15	0.89	0.41	< 0.01
Protein, kg/d	1.30	1.33	1.33	1.33	0.01	0.13	0.46	0.41	< 0.01
Lactose, %	4.63	4.65	4.63	4.63	0.01	0.98	0.27	0.51	< 0.01
Lactose, kg/d	1.82	1.85	1.84	1.84	0.02	0.34	0.50	0.71	< 0.01
PUN, mg/dL	9.11	9.13	9.04	8.89	0.17	0.42	0.42	0.72	< 0.01
ECM[4], kg/d	46.0	46.9	47.1	46.8	0.50	0.17	0.47	0.46	< 0.01
BW, kg	692	691	694	693	2.1	0.74	0.67	0.83	0.26
BW change, kg/d	0.16	0.27	0.16	0.44	0.09	**0.07**	0.33	**0.08**	-
BCS[6]	2.93	2.93	3.04	2.93	0.40	-	-	-	< 0.01

	Diet^1					P-value^2			
Item	CON	R11	R14.5	R18	SEM	Linear	Quad	Trt	Trt x Wk
Total FA, g/100 g milk	4.33	4.39	4.43	4.37	0.04	0.22	0.34	0.41	0.31
De novo^3									
g/100 g milk	1.13	1.16	1.17	1.16	0.01	0.05	0.32	0.17	0.35
g/d	438	452	458	454	6.3	0.06	0.46	0.21	0.06
g/100 g FA	26.1	26.4	26.2	26.3	0.11	0.24	0.54	0.41	< 0.01
Mixed^4									
g/100 g milk	1.85	1.88	1.91	1.90	0.02	0.02	0.79	0.10	0.07
g/d	720	737	753	746	11.8	0.09	0.76	0.28	< 0.01
g/100 g FA	42.8	42.9	43.0	43.1	0.18	0.25	0.66	0.64	< 0.01
Preformed^5									
g/100 g milk	1.34	1.35	1.36	1.33	0.02	0.95	0.27	0.61	< 0.01
g/d	520	527	533	521	7.1	0.61	0.28	0.54	< 0.01
g/100 g FA	31.0	30.7	30.8	30.6	0.21	0.15	0.98	0.46	< 0.01
Chain length	14.57	14.54	14.54	14.54	0.01	0.02	0.27	0.08	< 0.01

Milk de novo and mixed fatty acids from this study compared to Jersey milk components



Holstein vs. Jersey Farms 2019

De novo + mixed origin fatty acids and bulk tank milk fat

Similar slope and high R^2 for the strong relationship between de novo + mixed origin fatty acid concentration and bulk tank milk fat concentration for Jersey and Holstein bulk tank milk. (herd average days in milk 150 to 200 days)

Barbano et al. Proc Cornell Nutr. Conf. 2019

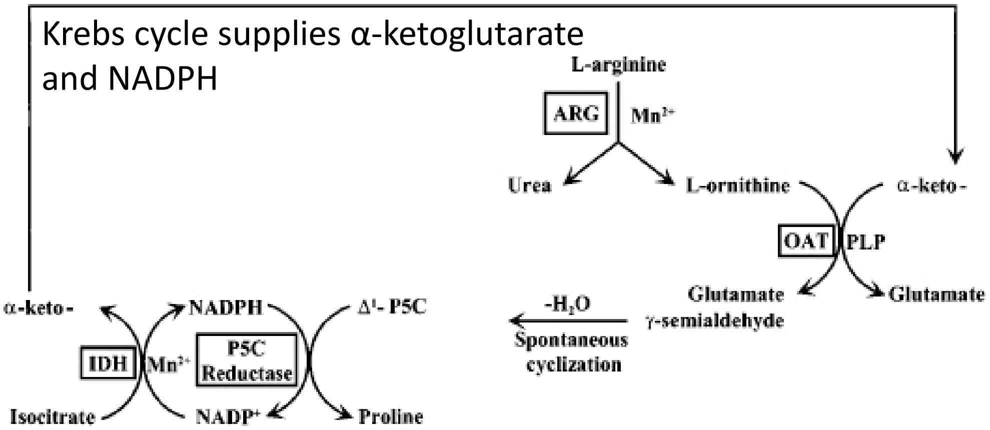
Amino Acid Composition of Casein and Bacterial Protein

Essential AA	Casein, g/kg [1]	Rumen bacteria, %TAA[2]	Non-essential AA	Casein, g/kg[1]	Rumen bacteria, %TAA[2]
Arg	38.6	4.8	Ala	32.1	7.4
His	28.8	1.9	Asn	39.8	----
Ile	**52.0**				11.9
Leu	**97.3**				----
Lys	81.8				12.2
Met	30.2	2.4	Gly	19.4	5.8
Phe	53.7	5.1	**Pro**	**110.8**	3.8
Thr	45.3	5.3	Ser	59.6	3.9
Trp	12.5	1.0	Tyr	57.5	4.9
Val	**59.2**	6.4			

Casein
BCAA 208.5 g/kg
Proline 110.8 g/kg

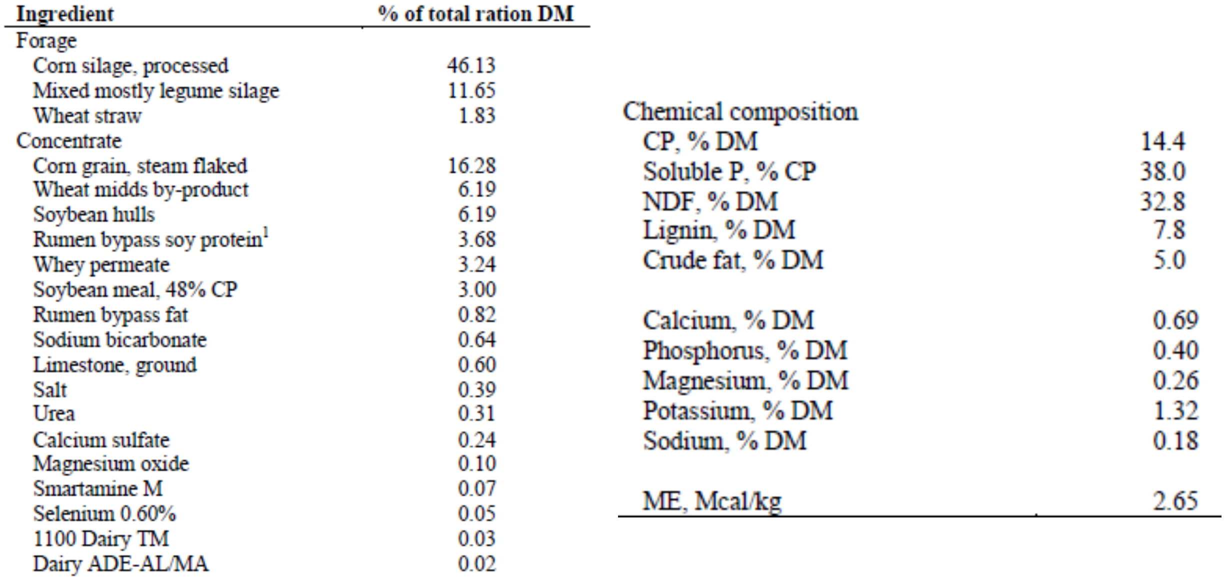
[1]Lapierre et al., 2012; [2]Fonseca et al., 2014

Proposed Proline production in the bovine mammary gland



Proposed mechanism of proline production in the lactating bovine mammary gland. IDH = isocitrate dehydrogenase, P5C = pyrroline-5-carboxylate, OAT = ornithine aminotransferase, α-keto = α-ketoglutarate, and ARG = arginase. From (Basch et al., 1997).

Abomasal Infusion Study to Evaluate Effects of Histidine and Proline Supply

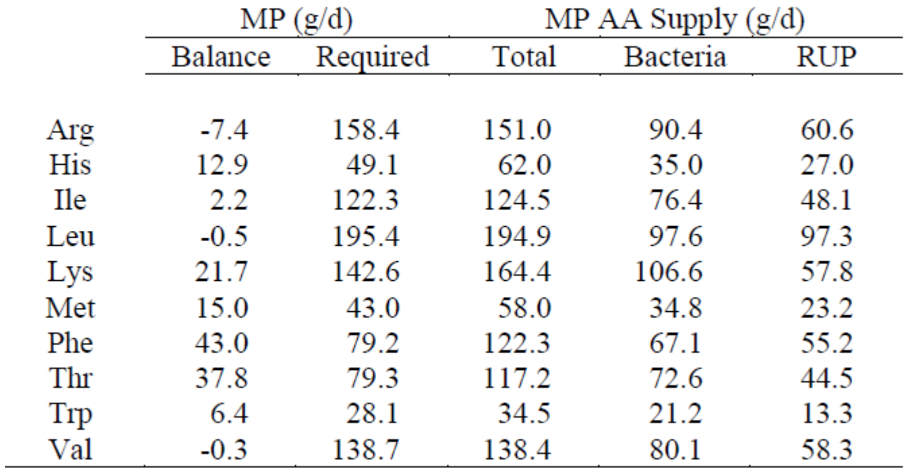


Ingredient	% of total ration DM
Forage	
Corn silage, processed	46.13
Mixed mostly legume silage	11.65
Wheat straw	1.83
Concentrate	
Corn grain, steam flaked	16.28
Wheat midds by-product	6.19
Soybean hulls	6.19
Rumen bypass soy protein[1]	3.68
Whey permeate	3.24
Soybean meal, 48% CP	3.00
Rumen bypass fat	0.82
Sodium bicarbonate	0.64
Limestone, ground	0.60
Salt	0.39
Urea	0.31
Calcium sulfate	0.24
Magnesium oxide	0.10
Smartamine M	0.07
Selenium 0.60%	0.05
1100 Dairy TM	0.03
Dairy ADE-AL/MA	0.02

Chemical composition	
CP, % DM	14.4
Soluble P, % CP	38.0
NDF, % DM	32.8
Lignin, % DM	7.8
Crude fat, % DM	5.0
Calcium, % DM	0.69
Phosphorus, % DM	0.40
Magnesium, % DM	0.26
Potassium, % DM	1.32
Sodium, % DM	0.18
ME, Mcal/kg	2.65

Hofherr, 2010

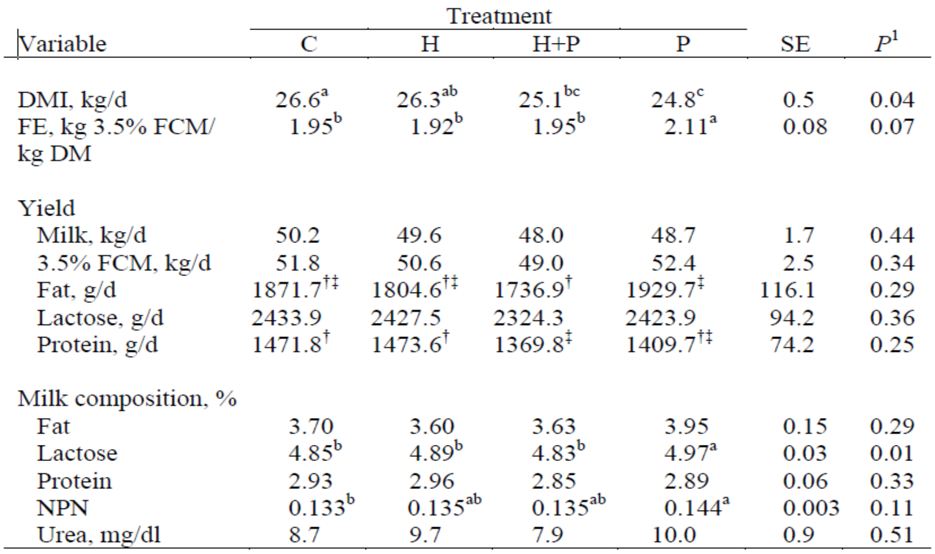
The formulated essential amino acid balance, requirement, and supply CNCPS v6.1 for a 635 kg cow consuming 22.6 kg DM/d and producing 39.9 kg milk/d at 3.65% fat and 3.01% protein – 10 g Histidine infused or 20 g Proline or the same amount of both AA



	MP (g/d)		MP AA Supply (g/d)		
	Balance	Required	Total	Bacteria	RUP
Arg	-7.4	158.4	151.0	90.4	60.6
His	12.9	49.1	62.0	35.0	27.0
Ile	2.2	122.3	124.5	76.4	48.1
Leu	-0.5	195.4	194.9	97.6	97.3
Lys	21.7	142.6	164.4	106.6	57.8
Met	15.0	43.0	58.0	34.8	23.2
Phe	43.0	79.2	122.3	67.1	55.2
Thr	37.8	79.3	117.2	72.6	44.5
Trp	6.4	28.1	34.5	21.2	13.3
Val	-0.3	138.7	138.4	80.1	58.3

Hofherr, 2010

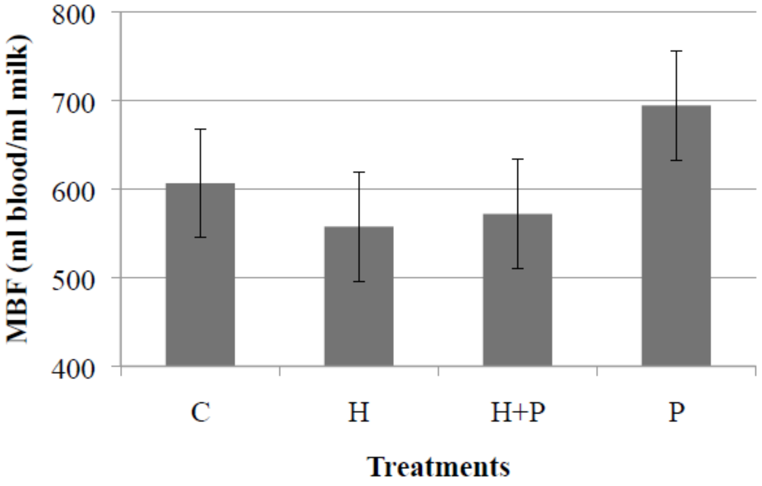
Least squares means for dry matter intake, feed efficiency (FE), milk yield, and milk composition of cows fed a common diet and infused abomasally with water (C), histidine (H), proline (P), or a combination of both AA (H+P).



Variable	Treatment C	Treatment H	Treatment H+P	Treatment P	SE	P^{1}
DMI, kg/d	26.6^{a}	26.3^{ab}	25.1^{bc}	24.8^{c}	0.5	0.04
FE, kg 3.5% FCM/ kg DM	1.95^{b}	1.92^{b}	1.95^{b}	2.11^{a}	0.08	0.07
Yield						
Milk, kg/d	50.2	49.6	48.0	48.7	1.7	0.44
3.5% FCM, kg/d	51.8	50.6	49.0	52.4	2.5	0.34
Fat, g/d	$1871.7^{\dagger\ddagger}$	$1804.6^{\dagger\ddagger}$	$1736.9^{\dagger}$	$1929.7^{\ddagger}$	116.1	0.29
Lactose, g/d	2433.9	2427.5	2324.3	2423.9	94.2	0.36
Protein, g/d	$1471.8^{\dagger}$	$1473.6^{\dagger}$	$1369.8^{\ddagger}$	$1409.7^{\dagger\ddagger}$	74.2	0.25
Milk composition, %						
Fat	3.70	3.60	3.63	3.95	0.15	0.29
Lactose	4.85^{b}	4.89^{b}	4.83^{b}	4.97^{a}	0.03	0.01
Protein	2.93	2.96	2.85	2.89	0.06	0.33
NPN	0.133^{b}	0.135^{ab}	0.135^{ab}	0.144^{a}	0.003	0.11
Urea, mg/dl	8.7	9.7	7.9	10.0	0.9	0.51

Hofherr, 2010

Mammary blood flow for each of the four treatments. Blood flow estimated using the Fick Principle and Phe and Tyr as markers, is expressed as ml of blood per ml of milk, and values represent the LS mean ± SE.



Hofherr, 2010

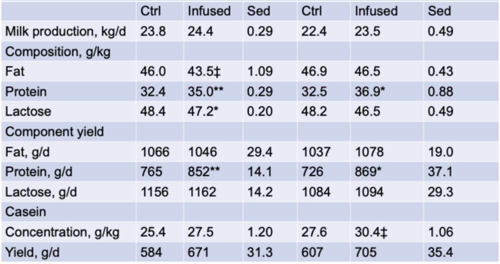
Past AA Infusion Studies

Milk Protein AA Profile Jugular Infusions			
EAA	**Infusion (g/d)**	**NEAA**	**Infusion (g/d)**
Arg	12.8	Ala	12.4
His	10.2	Asn	17.6
Ile	22.4	Asp	13.0
Leu	36.7	Cys	2.9
Lys	31.0	Glu	43.4
Met	10.7	Gln	35.1
Phe	36.7	Gly	6.5
Thr	16.5	Pro	37.6
Trp	5.5	Ser	23.7
Val	24.9	Tyr	0.4
Total	207.8	Total	192.2

Metcalf et al., 1996

- 4 Holstein Cows, Mid Lactation, Jugular Infusion
- 4 d saline (control) followed by 5 d mix (TAA or EAA)
- Trt Diet: 87% CP and 104% ME
- Control Diet: 104% MP and 106% ME
- % MP reqts with trts : 120% (TAA) and 108% (EAA)

Comparison of milk production, component output, and composition in response to AA infusions. Metcalf et al., 1996



	TAA			EAA		
	Ctrl	Infused	Sed	Ctrl	Infused	Sed
Milk production, kg/d	23.8	24.4	0.29	22.4	23.5	0.49
Composition, g/kg						
Fat	46.0	43.5‡	1.09	46.9	46.5	0.43
Protein	32.4	35.0**	0.29	32.5	36.9*	0.88
Lactose	48.4	47.2*	0.20	48.2	46.5	0.49
Component yield						
Fat, g/d	1066	1046	29.4	1037	1078	19.0
Protein, g/d	765	852**	14.1	726	869*	37.1
Lactose, g/d	1156	1162	14.2	1084	1094	29.3
Casein						
Concentration, g/kg	25.4	27.5	1.20	27.6	30.4‡	1.06
Yield, g/d	584	671	31.3	607	705	35.4

Comparison of milk production, component output, and composition in response to AA infusions. Metcalf et al., 1996

	TAA			EAA		
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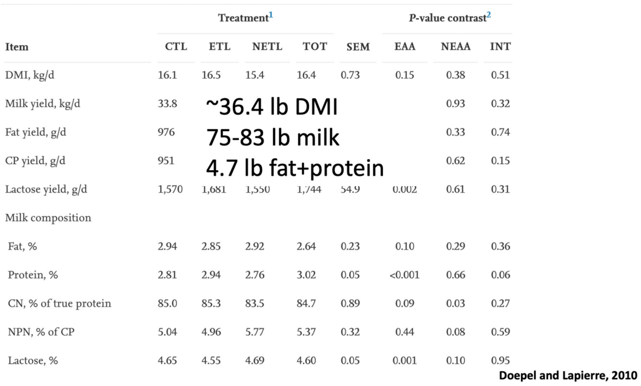
Casein AA Profile, 3:1 Lys:Met
Abomasal Infusions

EAA	Infusion (g/d)	NEAA	Infusion (g/d)
Arg	24.1	Ala	20.7
His	19.1	Asn	26.4
Ile	41.8	Asp	21.3
Leu	69.5	Cys	4.4
Lys	58.8	Gln	93.0
Met	23.0	Glu (Gln)	41.7
Phe	24.7	Gly	11.3
Thr	30.5	Pro	62.6
Trp	10.6	Ser	39.5
Val	46.8	Tyr (Phe)	0
Total	358.9	Total	192.2

Doepel and Lapierre, 2010

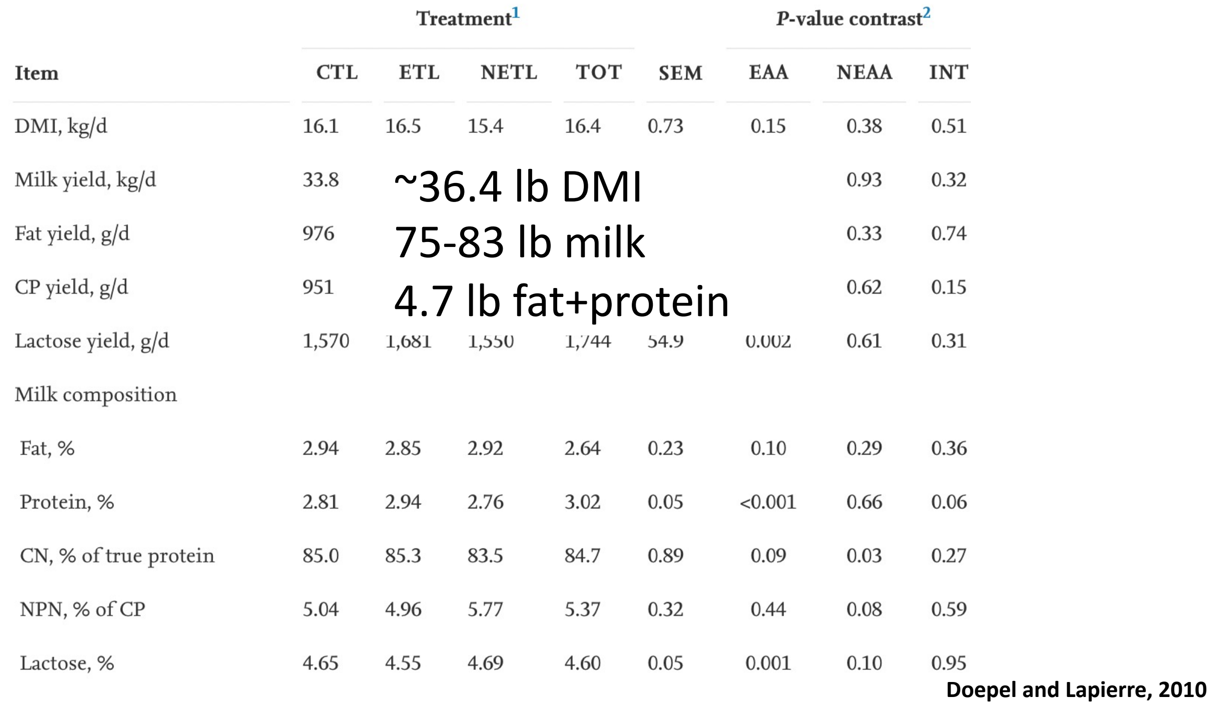
- 8 Holstein Cows, 61 DIM, Abomasal Infusion
  - 4 Trts: Control, EAA, NEAA, TAA
    - 72% MP and 100% NE_L



	Treatment[1]					*P*-value contrast[2]		
Item	CTL	ETL	NETL	TOT	SEM	EAA	NEAA	INT
DMI, kg/d	16.1	16.5	15.4	16.4	0.73	0.15	0.38	0.51
Milk yield, kg/d	33.8						0.93	0.32
Fat yield, g/d	976						0.33	0.74
CP yield, g/d	951						0.62	0.15
Lactose yield, g/d	1,570	1,681	1,550	1,744	54.9	0.002	0.61	0.31
Milk composition								
Fat, %	2.94	2.85	2.92	2.64	0.23	0.10	0.29	0.36
Protein, %	2.81	2.94	2.76	3.02	0.05	<0.001	0.66	0.06
CN, % of true protein	85.0	85.3	83.5	84.7	0.89	0.09	0.03	0.27
NPN, % of CP	5.04	4.96	5.77	5.37	0.32	0.44	0.08	0.59
Lactose, %	4.65	4.55	4.69	4.60	0.05	0.001	0.10	0.95

~36.4 lb DMI
75-83 lb milk
4.7 lb fat+protein

Doepel and Lapierre, 2010



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Milk yield, kg/d	33.8						0.93	0.32
Fat yield, g/d	976						0.33	0.74
CP yield, g/d	951						0.62	0.15
Lactose yield, g/d	1,570	1,681	1,550	1,744	54.9	0.002	0.61	0.31
Milk composition								
Fat, %	2.94	2.85	2.92	2.64	0.23	0.10	0.29	0.36
Protein, %	2.81	2.94	2.76	3.02	0.05	<0.001	0.66	0.06
CN, % of true protein	85.0	85.3	83.5	84.7	0.89	0.09	0.03	0.27
NPN, % of CP	5.04	4.96	5.77	5.37	0.32	0.44	0.08	0.59
Lactose, %	4.65	4.55	4.69	4.60	0.05	0.001	0.10	0.95

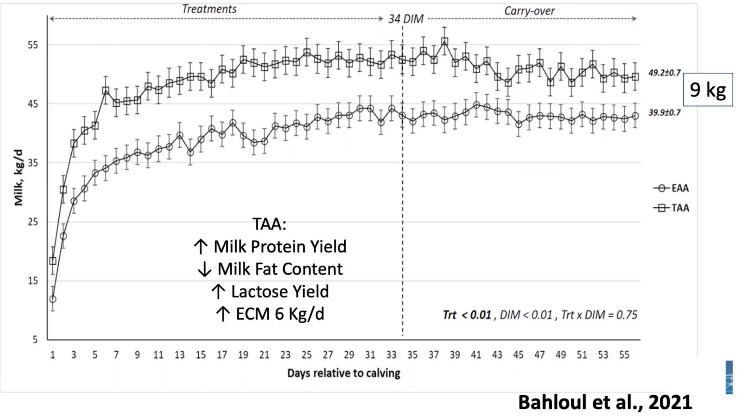
~36.4 lb DMI
75-83 lb milk
4.7 lb fat+protein

Doepel and Lapierre, 2010

Non-Essential AA Infusions in Fresh Cows

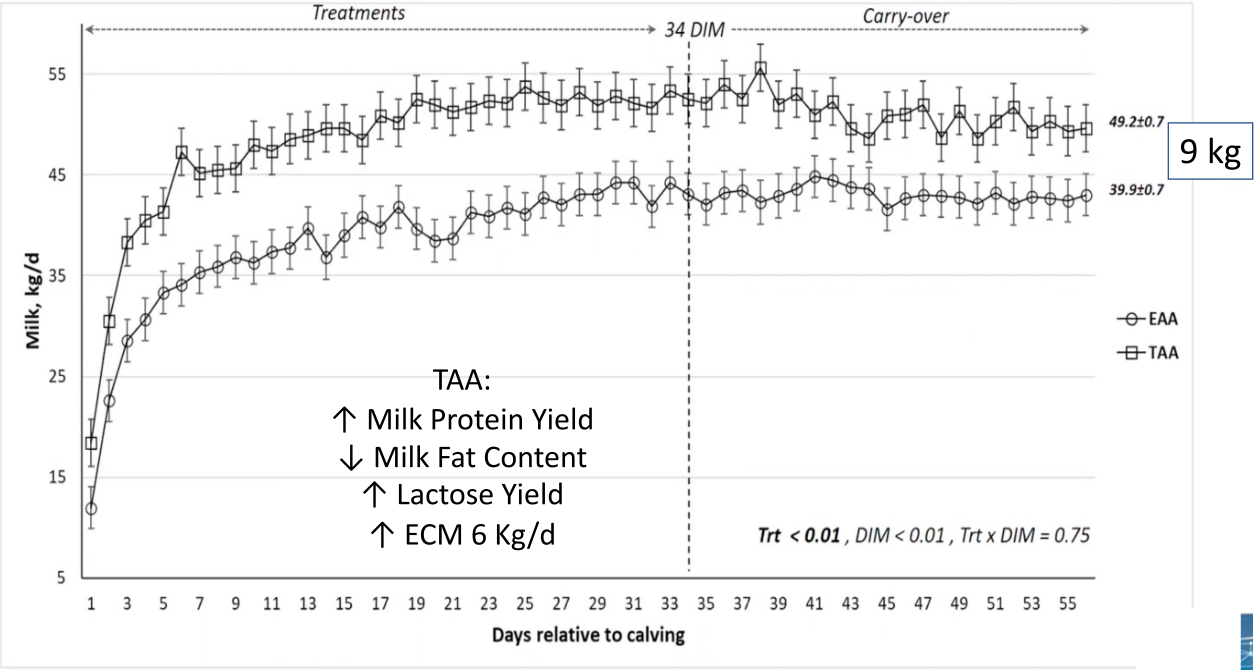
Bahloul et al., 2021

- 9 Holstein Cows, Calving to 50 DIM
- 2 Trts: TAA or EAA, Casein AA Profile
- Abomasal infusions



TAA:
↑ Milk Protein Yield
↓ Milk Fat Content
↑ Lactose Yield
↑ ECM 6 Kg/d

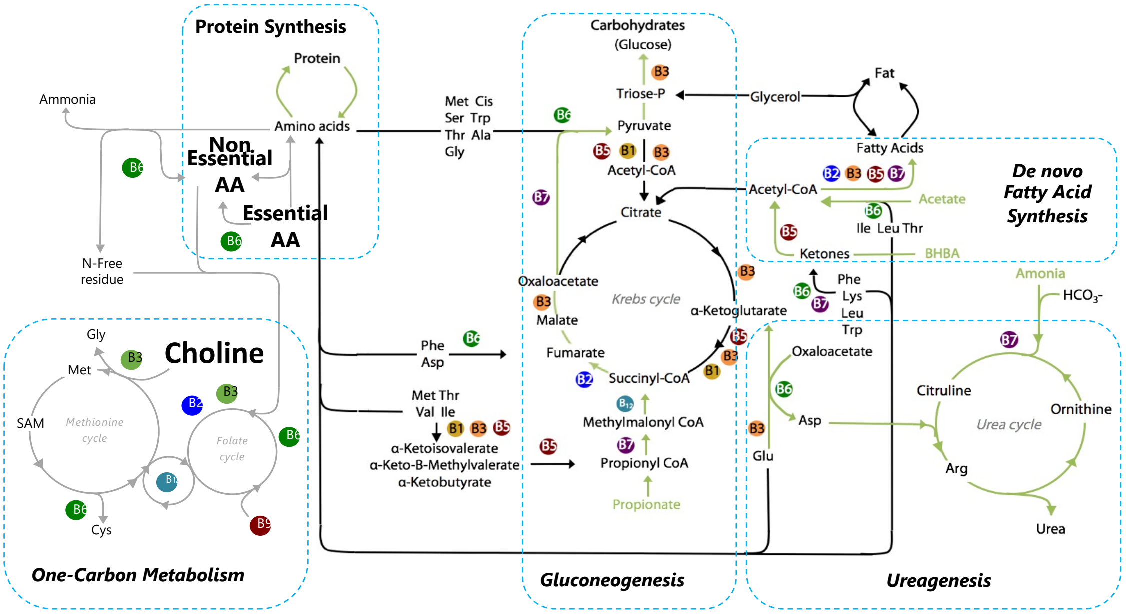
Bahloul et al., 2021



TAA:
↑ Milk Protein Yield
↓ Milk Fat Content
↑ Lactose Yield
↑ ECM 6 Kg/d

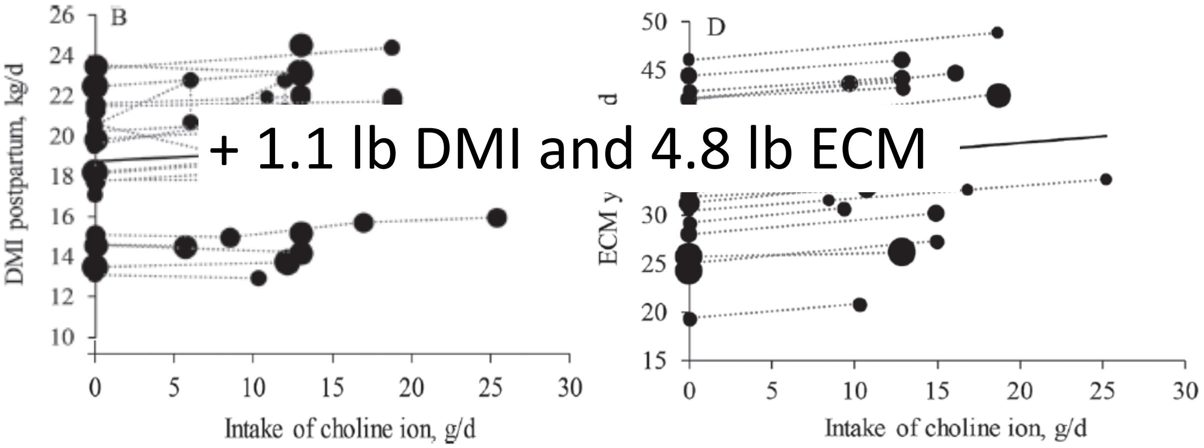
Bahloul et al., 2021

Intermediary Metabolism: B-Vitamins in a Transition Calf



Molano, 2020

Meta-analysis of the effects of supplemental choline during the transition period on performance and health of parous dairy cows – Arshad et al 2020



+ 1.1 lb DMI and 4.8 lb ECM

Summary

- The data would suggest that high producing dairy cattle have requirements for nutrients that are deemed "non-essential"
- As productivity increases, or at different stages of lactation, nutrient resources become more limiting for all pathways, and this could be energy, AA or something like a methyl donor
- Terms like metabolizable protein will remain useful as it captures the supply of NEAA
- We need to consider non-essential nutrients like required nutrients and start to describe the requirements in nutrition models

Thank you for your attention

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