Histidine – a limiting amino acid for dairy cows

Alex N. Hristov
Distinguished Professor, Department of Animal Science
The Pennsylvania State University

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Talk outline

- How it all started - feeding reduced-protein diets to dairy cows
- Why Histidine?
- Early research
- Penn State research
- Conclusions

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Low-protein diets - Why?

- What is a low-protein diet?
  - Diets supplying MP below requirements?
  - Diets with CP below “industry standards”?
  - Several surveys showed average CP in dairy diets being around **17%; now many diets tend to be closer to 16%**
- **Reasons for feeding low-protein diets:**
  - Reduced feed cost
  - Striving for efficiency
  - Reduced N emissions (originally, NH_3 was the target)
  - Protein overfeeding and reproduction

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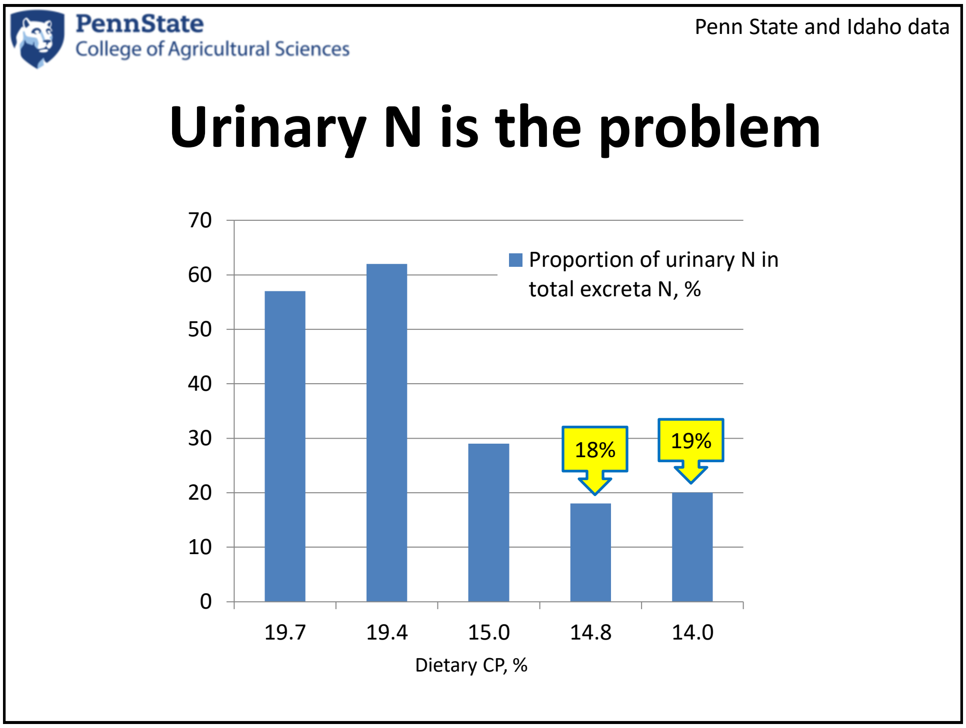
Environmental concerns with N

- Eutrophication of water bodies
- Ground water quality
- Air pollution



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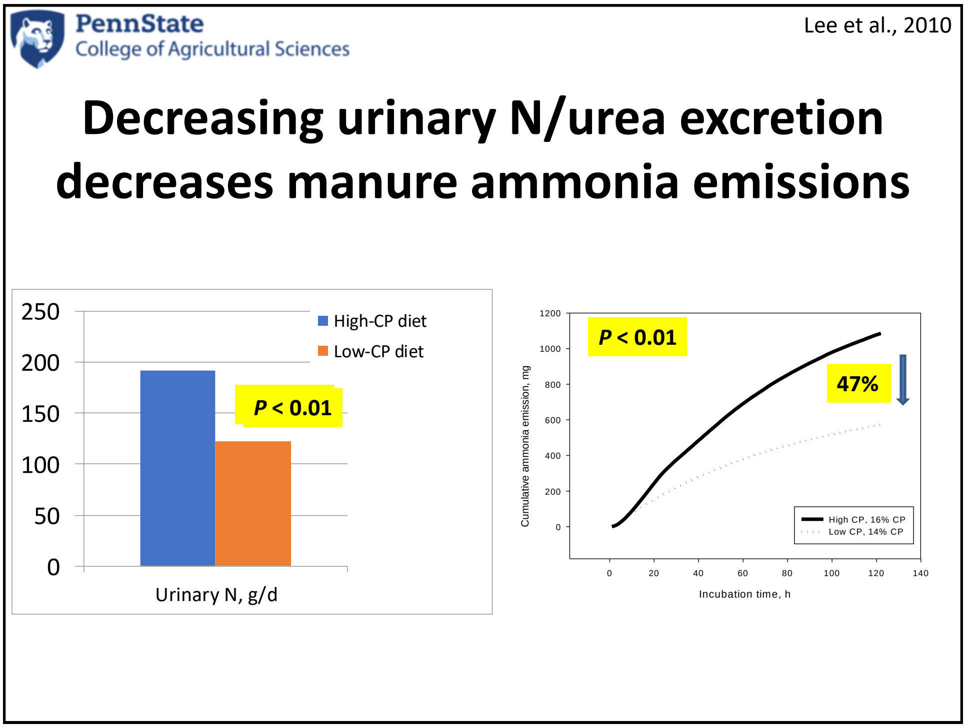
Penn State and Idaho data

Urinary N is the problem



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Lee et al., 2010

Decreasing urinary N/urea excretion decreases manure ammonia emissions

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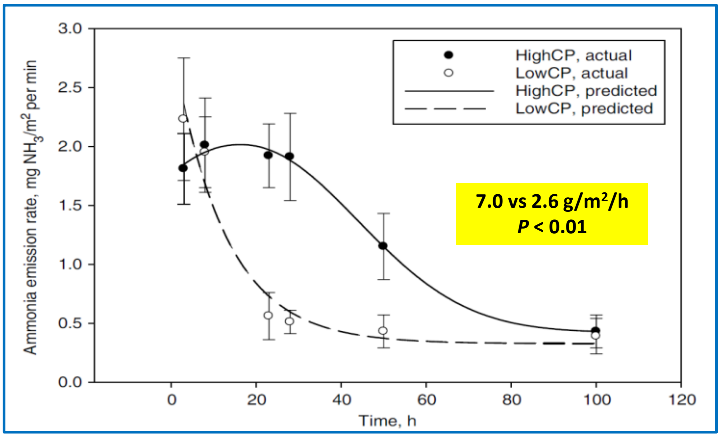
Lee et al., 2016

Dietary CP influences manure ammonia emissions as well



7.0 vs 2.6 g/m^2/h
$P < 0.01$

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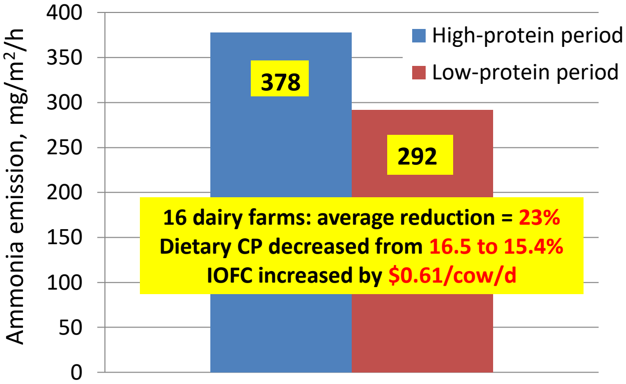
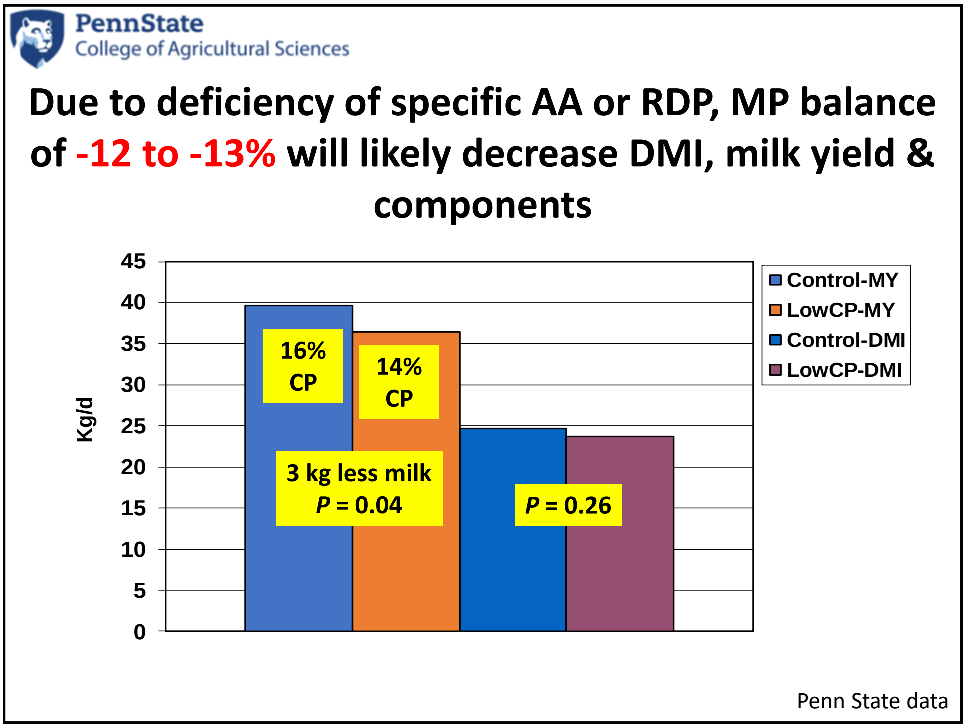
1%-unit reduction in CP can have a large effect on ammonia emission from manure



16 dairy farms: average reduction = 23%
Dietary CP decreased from 16.5 to 15.4%
IOFC increased by $0.61/cow/d

Hristov et al., 2015



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Due to deficiency of specific AA or RDP, MP balance of -12 to -13% will likely decrease DMI, milk yield & components

Penn State data

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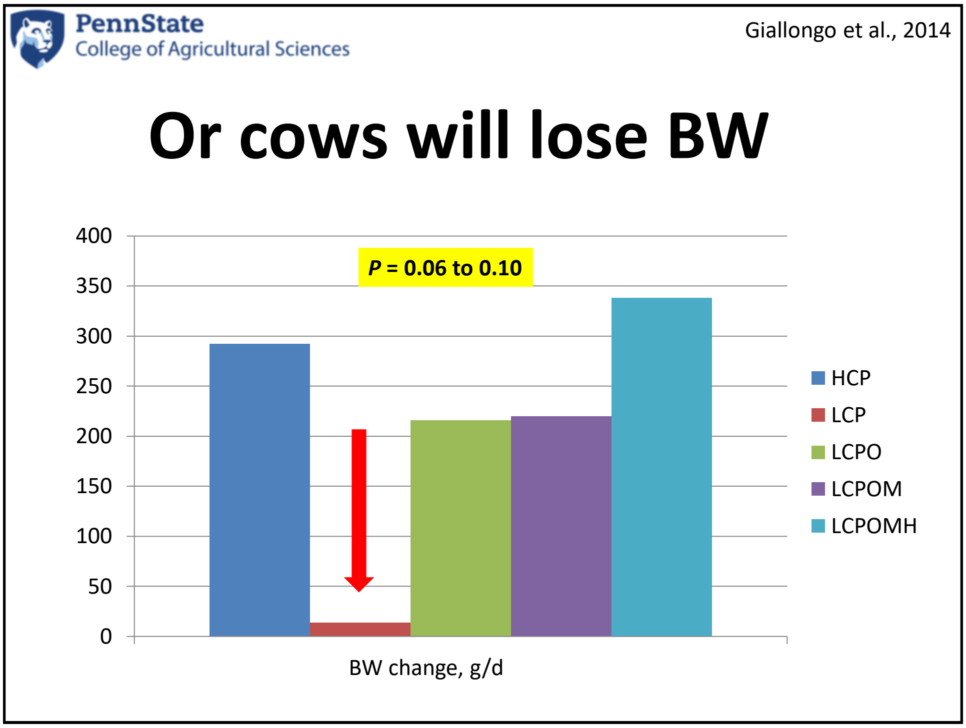

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Giallongo et al., 2014

Or cows will lose BW

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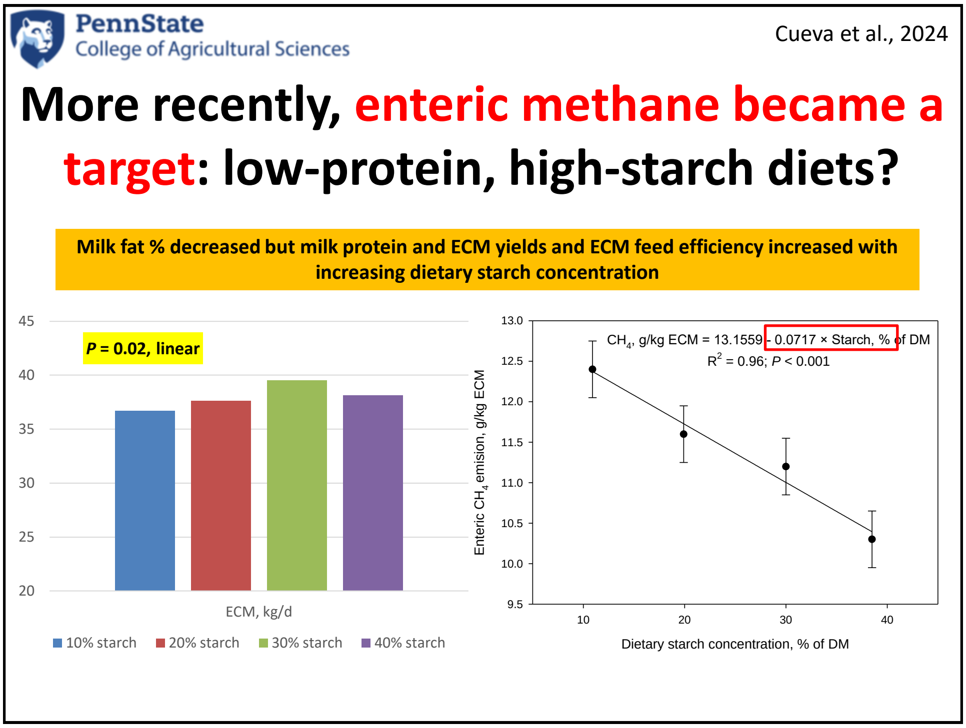

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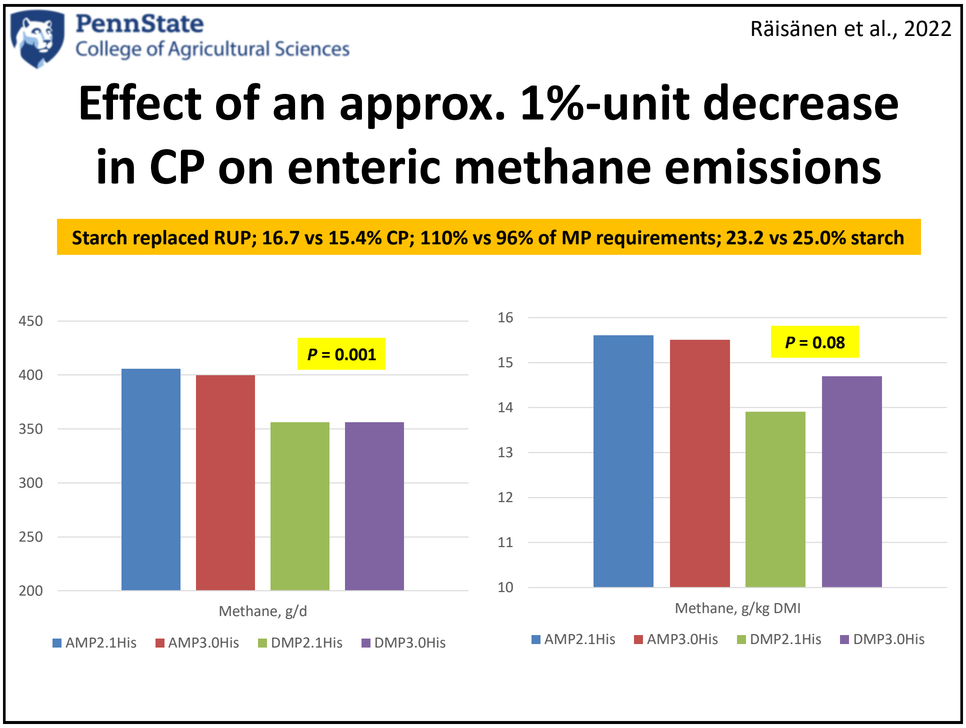
Cueva et al., 2024

More recently, enteric methane became a target: low-protein, high-starch diets?

Milk fat % decreased but milk protein and ECM yields and ECM feed efficiency increased with increasing dietary starch concentration



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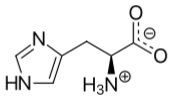
Räisänen et al., 2022

Effect of an approx. 1%-unit decrease in CP on enteric methane emissions

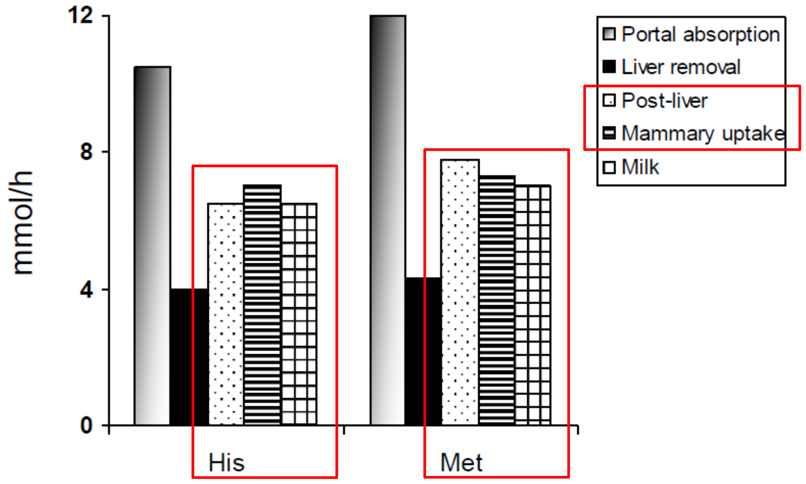
Starch replaced RUP; 16.7 vs 15.4% CP; 110% vs 96% of MP requirements; 23.2 vs 25.0% starch

Histidine



- Unique among EAA with an imidazole side chain
- Similar to Met, a Group 1 AA (extracted by the liver with post-liver supply approx. equal to mammary uptake and output in milk)
- Which would suggest that requirements for His should be similar to those for Met
- However, variability in estimates for His requirements have been large: 2.2 to >3% of MP
  - Major reasons for this are endogenous His depots: carnosine and blood hemoglobin
  - And lower His than Met in microbial protein

Net flux of Met and His



Lapierre et al., 2008

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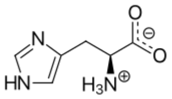
Histidine



- Catabolic pathways:
  - Incorporation into protein
  - Synthesis of carnosine
  - Decarboxylation of histidine to histamine by histidine decarboxylase
  - Buffering role of histidine and histidine-related compounds
- Controversial effects of His on feed intake regulation
  - Reports with lab animals and non-ruminants indicate stimulatory effect on feed intake: perhaps through acting on the anterior prepyriform cortex, the brain's AA "chemosensor" (no stimulation when His was infused in the jugular veins vs. the carotid arteries)
  - Other reports suggest the opposite effect – His depresses feed intake through its conversion into histamine in the hypothalamus; the released histamine acts on food intake through histamine H1 receptors activation of histamine neurons

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Räisänen et al., 2023

Histidine research

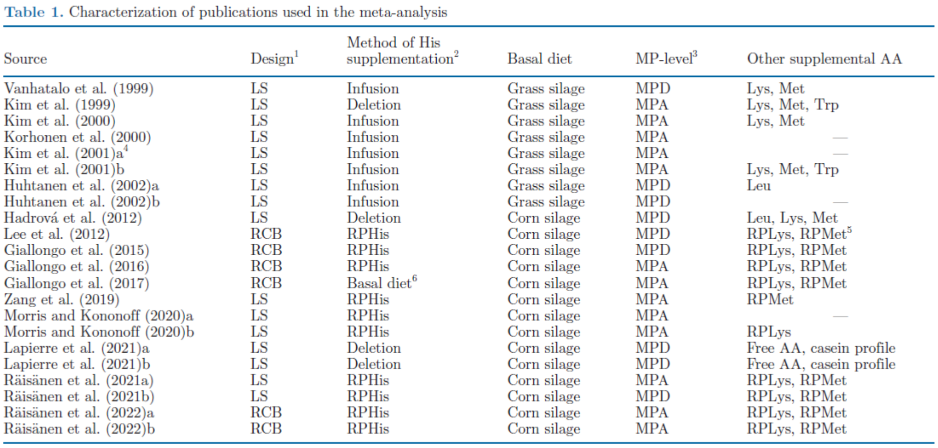

Table 1. Characterization of publications used in the meta-analysis

Source	Design^{1}	Method of His supplementation^{2}	Basal diet	MP-level^{3}	Other supplemental AA
Vanhatalo et al. (1999)	LS	Infusion	Grass silage	MPD	Lys, Met
Kim et al. (1999)	LS	Deletion	Grass silage	MPA	Lys, Met, Trp
Kim et al. (2000)	LS	Infusion	Grass silage	MPA	Lys, Met
Korhonen et al. (2000)	LS	Infusion	Grass silage	MPA	—
Kim et al. (2001)a^{4}	LS	Infusion	Grass silage	MPA	—
Kim et al. (2001)b	LS	Infusion	Grass silage	MPA	Lys, Met, Trp
Huhtanen et al. (2002)a	LS	Infusion	Grass silage	MPD	Leu
Huhtanen et al. (2002)b	LS	Infusion	Grass silage	MPD	—
Hadrová et al. (2012)	LS	Deletion	Corn silage	MPD	Leu, Lys, Met
Lee et al. (2012)	RCB	RPHis	Corn silage	MPD	RPLys, RPMet^{5}
Giallongo et al. (2015)	RCB	RPHis	Corn silage	MPD	RPLys, RPMet
Giallongo et al. (2016)	RCB	RPHis	Corn silage	MPA	RPLys, RPMet
Giallongo et al. (2017)	RCB	Basal diet^{6}	Corn silage	MPA	RPLys, RPMet
Zang et al. (2019)	LS	RPHis	Corn silage	MPA	RPMet
Morris and Kononoff (2020)a	LS	RPHis	Corn silage	MPA	—
Morris and Kononoff (2020)b	LS	RPHis	Corn silage	MPA	RPLys
Lapierre et al. (2021)a	LS	Deletion	Corn silage	MPD	Free AA, casein profile
Lapierre et al. (2021)b	LS	Deletion	Corn silage	MPD	Free AA, casein profile
Räisänen et al. (2021a)	LS	RPHis	Corn silage	MPA	RPLys, RPMet
Räisänen et al. (2021b)	LS	RPHis	Corn silage	MPD	RPLys, RPMet
Räisänen et al. (2022)a	RCB	RPHis	Corn silage	MPA	RPLys, RPMet
Räisänen et al. (2022)b	RCB	RPHis	Corn silage	MPA	RPLys, RPMet

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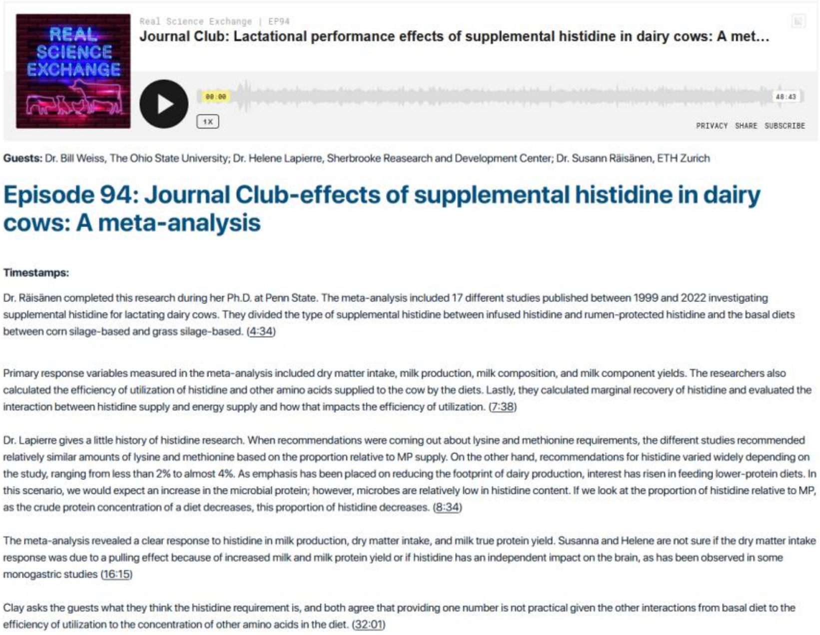

Journal Club: Lactational performance effects of supplemental histidine in dairy cows: A met...

Guests: Dr. Bill Weiss, The Ohio State University; Dr. Helene Lapierre, Sherbrooke Reasearch and Development Center; Dr. Susann Räisänen, ETH Zurich

Episode 94: Journal Club-effects of supplemental histidine in dairy cows: A meta-analysis

Timestamps:

Dr. Räisänen completed this research during her Ph.D. at Penn State. The meta-analysis included 17 different studies published between 1999 and 2022 investigating supplemental histidine for lactating dairy cows. They divided the type of supplemental histidine between infused histidine and rumen-protected histidine and the basal diets between corn silage-based and grass silage-based. (4:34)

Primary response variables measured in the meta-analysis included dry matter intake, milk production, milk composition, and milk component yields. The researchers also calculated the efficiency of utilization of histidine and other amino acids supplied to the cow by the diets. Lastly, they calculated marginal recovery of histidine and evaluated the interaction between histidine supply and energy supply and how that impacts the efficiency of utilization. (7:38)

Dr. Lapierre gives a little history of histidine research. When recommendations were coming out about lysine and methionine requirements, the different studies recommended relatively similar amounts of lysine and methionine based on the proportion relative to MP supply. On the other hand, recommendations for histidine varied widely depending on the study, ranging from less than 2% to almost 4%. As emphasis has been placed on reducing the footprint of dairy production, interest has risen in feeding lower-protein diets. In this scenario, we would expect an increase in the microbial protein; however, microbes are relatively low in histidine content. If we look at the proportion of histidine relative to MP, as the crude protein concentration of a diet decreases, this proportion of histidine decreases. (8:34)

The meta-analysis revealed a clear response to histidine in milk production, dry matter intake, and milk true protein yield. Susanna and Helene are not sure if the dry matter intake response was due to a pulling effect because of increased milk and milk protein yield or if histidine has an independent impact on the brain, as has been observed in some monogastric studies (16:15)

Clay asks the guests what they think the histidine requirement is, and both agree that providing one number is not practical given the other interactions from basal diet to the efficiency of utilization to the concentration of other amino acids in the diet. (32:01)

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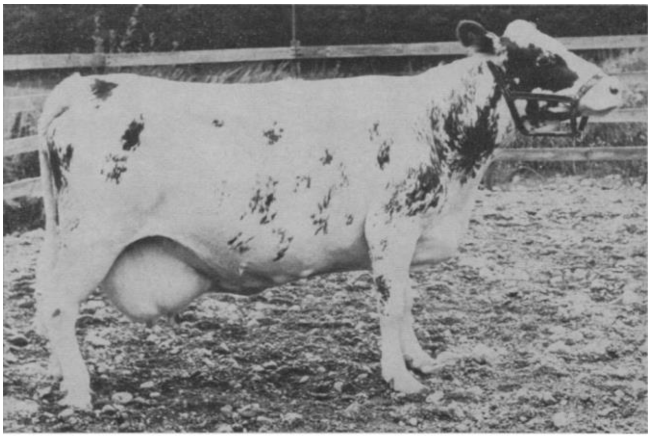
Milk Production of Cows on Protein-Free Feed

Studies of the use of urea and ammonium salts as the sole nitrogen source open new important perspectives.

Artturi I. Virtanen



Science, 1966

Fig. 3. Test cow Metta after being on test feed 370 days from calving.

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A. I. Virtanen; Science, 1966

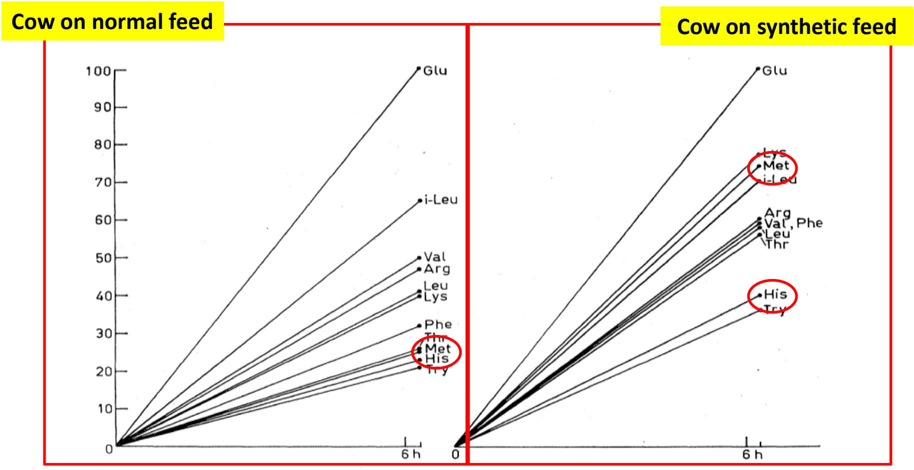

Fig. 1. Labeling of the essential amino acids of total milk protein 6.3 hours after the cow had been fed a single dose of ^{15}N-urea. The results are expressed as a percentage of the labeling of glutamic acid. At left, results of a feeding experiment with a cow on normal feed (17 March 1966); at right, results of a feeding experiment with a test cow (20 October 1962) 6 months after the start of the experimental feeding. Histidine and tryptophan have the lowest labeling in both experiments, but the increase in their labeling in the cow on the experimental feed is remarkable. [Determinations by M. Kreula and T. Moisio]

Broderick, 1972

Ranking of AA limiting milk production of a cow milking 35 kg/d with 3.30% CP

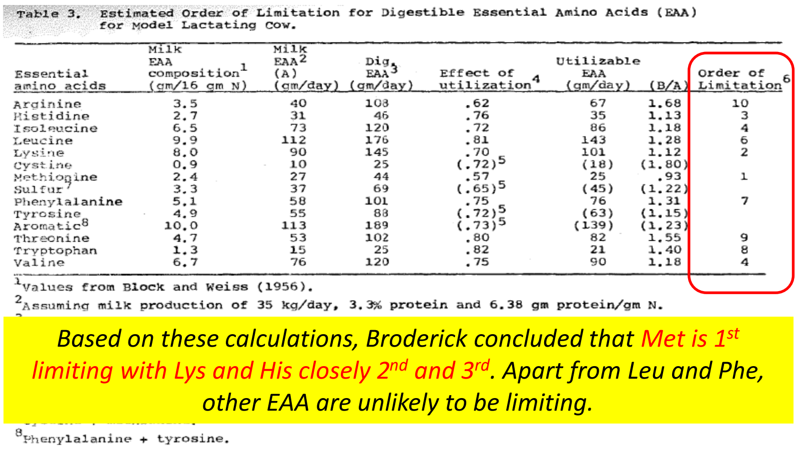

Table 3. Estimated Order of Limitation for Digestible Essential Amino Acids (EAA) for Model Lactating Cow.

Essential amino acids	Milk EAA composition[1] (gm/16 gm N)	Milk EAA[2] (A) (gm/day)	Dig. EAA[3] (gm/day)	Effect of utilization[4]	Utilizable EAA (gm/day)	(B/A)	Order of Limitation[6]
Arginine	3.5	40	108	.62	67	1.68	10
Histidine	2.7	31	46	.76	35	1.13	3
Isoleucine	6.5	73	120	.72	86	1.18	4
Leucine	9.9	112	176	.81	143	1.28	6
Lysine	8.0	90	145	.70	101	1.12	2
Cystine	0.9	10	25	(.72)[5]	(18)	(1.80)	
Methionine	2.4	27	44	.57	25	.93	1
Sulfur[7]	3.3	37	69	(.65)[5]	(45)	(1.22)	
Phenylalanine	5.1	58	101	.75	76	1.31	7
Tyrosine	4.9	55	88	(.72)[5]	(63)	(1.15)	
Aromatic[8]	10.0	113	189	(.73)[5]	(139)	(1.23)	
Threonine	4.7	53	102	.80	82	1.55	9
Tryptophan	1.3	15	25	.82	21	1.40	8
Valine	6.7	76	120	.75	90	1.18	4

[1] Values from Block and Weiss (1956).

[2] Assuming milk production of 35 kg/day, 3.3% protein and 6.38 gm protein/gm N.

Based on these calculations, Broderick concluded that Met is 1st limiting with Lys and His closely 2nd and 3rd. Apart from Leu and Phe, other EAA are unlikely to be limiting.

[8] Phenylalanine + tyrosine.

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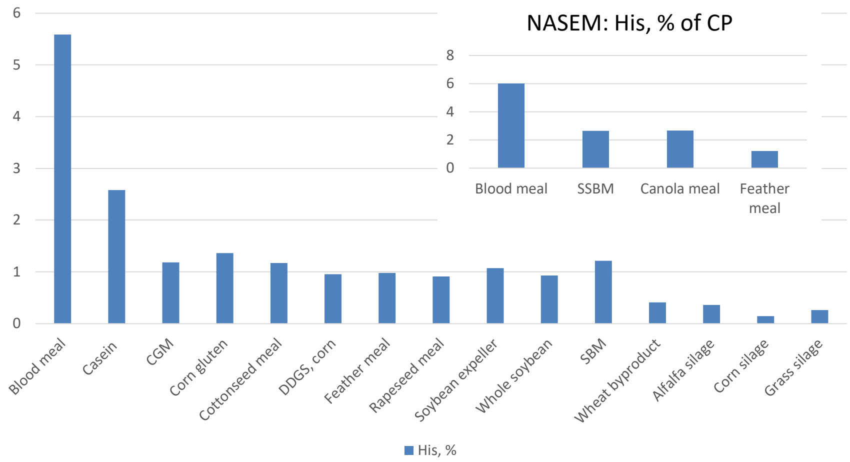
Evonik AMINODat

Histidine content in feeds



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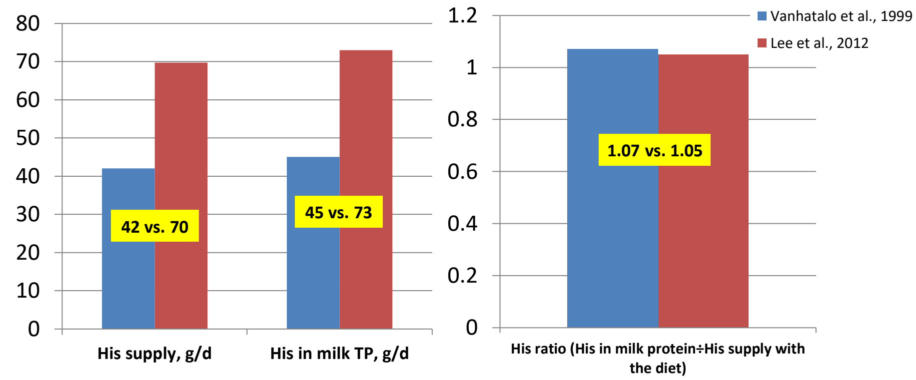
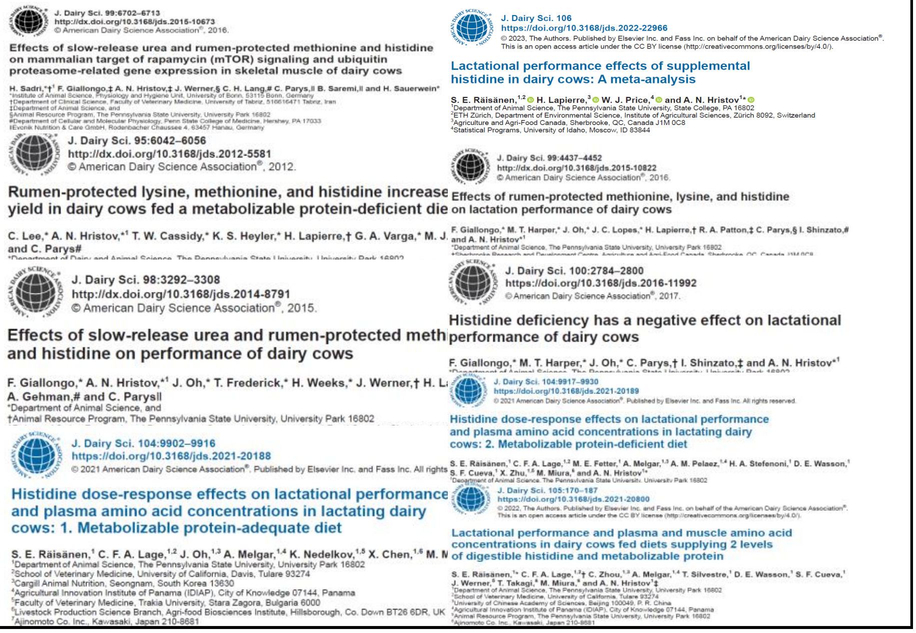
Can His be limiting on CS-based diets?

His supply ÷ output in grass- vs. corn silage-based diets



Histidine work at Penn State



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Effects of slow-release urea and rumen-protected methionine and histidine on mammalian target of rapamycin (mTOR) signaling and ubiquitin proteasome-related gene expression in skeletal muscle of dairy cows

H. Sadri,*†[1] F. Giallongo,‡ A. N. Hristov,‡ J. Werner,§ C. H. Lang,# C. Parys,‖ B. Saremi,‖ and H. Sauerwein*
*Institute of Animal Science, Physiology and Hygiene Unit, University of Bonn, 53115 Bonn, Germany
†Department of Clinical Science, Faculty of Veterinary Medicine, University of Tabriz, 516616471 Tabriz, Iran
‡Department of Animal Science, and
§Animal Resource Program, The Pennsylvania State University, University Park 16802
#Department of Cellular and Molecular Physiology, Penn State College of Medicine, Hershey, PA 17033
‖Evonik Nutrition & Care GmbH, Rodenbacher Chaussee 4, 63457 Hanau, Germany

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Rumen-protected lysine, methionine, and histidine increase yield in dairy cows fed a metabolizable protein-deficient die

C. Lee,* A. N. Hristov,*[1] T. W. Cassidy,* K. S. Heyler,* H. Lapierre,† G. A. Varga,* M. J.
and C. Parys#
*Department of Dairy and Animal Science, The Pennsylvania State University, University Park 16802

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Effects of slow-release urea and rumen-protected meth and histidine on performance of dairy cows

F. Giallongo,* A. N. Hristov,*[1] J. Oh,* T. Frederick,* H. Weeks,* J. Werner,† H. L
A. Gehman,# and C. Parys‖
*Department of Animal Science, and
†Animal Resource Program, The Pennsylvania State University, University Park 16802

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Histidine dose-response effects on lactational performance and plasma amino acid concentrations in lactating dairy cows: 1. Metabolizable protein-adequate diet

S. E. Räisänen,[1] C. F. A. Lage,[1,2] J. Oh,[1,3] A. Melgar,[1,4] K. Nedelkov,[1,5] X. Chen,[1,6] M. M
[1]Department of Animal Science, The Pennsylvania State University, University Park 16802
[2]School of Veterinary Medicine, University of California, Davis, Tulare 93274
[3]Cargill Animal Nutrition, Seongnam, South Korea 13630
[4]Agricultural Innovation Institute of Panama (IDIAP), City of Knowledge 07144, Panama
[5]Faculty of Veterinary Medicine, Trakia University, Stara Zagora, Bulgaria 6000
[6]Livestock Production Science Branch, Agri-food Biosciences Institute, Hillsborough, Co. Down BT26 6DR, UK
[7]Ajinomoto Co. Inc., Kawasaki, Japan 210-8681

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Lactational performance effects of supplemental histidine in dairy cows: A meta-analysis

S. E. Räisänen,[1,2] H. Lapierre,[3] W. J. Price,[4] and A. N. Hristov[1]*
[1]Department of Animal Science, The Pennsylvania State University, State College, PA 16802
[2]ETH Zürich, Department of Environmental Science, Institute of Agricultural Sciences, Zürich 8092, Switzerland
[3]Agriculture and Agri-Food Canada, Sherbrooke, QC, Canada J1M 0C8
[4]Statistical Programs, University of Idaho, Moscow, ID 83844

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Effects of rumen-protected methionine, lysine, and histidine on lactation performance of dairy cows

F. Giallongo,* M. T. Harper,* J. Oh,* J. C. Lopes,* H. Lapierre,† R. A. Patton,‡ C. Parys,§ I. Shinzato,# and A. N. Hristov*[1]
*Department of Animal Science, The Pennsylvania State University, University Park 16802
†Sherbrooke Research and Development Centre, Agriculture and Agri-Food Canada, Sherbrooke, QC, Canada J1M 0C8

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Histidine deficiency has a negative effect on lactational performance of dairy cows

F. Giallongo,* M. T. Harper,* J. Oh,* C. Parys,† I. Shinzato,‡ and A. N. Hristov*[1]
*Department of Animal Science, The Pennsylvania State University, University Park 16802

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Histidine dose-response effects on lactational performance and plasma amino acid concentrations in lactating dairy cows: 2. Metabolizable protein-deficient diet

S. E. Räisänen,[1] C. F. A. Lage,[1,2] M. E. Fetter,[1] A. Melgar,[1,3] A. M. Pelaez,[1,4] H. A. Stefenoni,[1] D. E. Wasson,[1] S. F. Cueva,[1] X. Zhu,[1,5] M. Miura,[6] and A. N. Hristov[1]*
[1]Department of Animal Science, The Pennsylvania State University, University Park 16802

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Lactational performance and plasma and muscle amino acid concentrations in dairy cows fed diets supplying 2 levels of digestible histidine and metabolizable protein

S. E. Räisänen,[1]* C. F. A. Lage,[1,2]† C. Zhou,[1,3] A. Melgar,[1,4] T. Silvestre,[1] D. E. Wasson,[1] S. F. Cueva,[1] J. Werner,[5] T. Takagi,[6] M. Miura,[6] and A. N. Hristov[1]‡
[1]Department of Animal Science, The Pennsylvania State University, University Park 16802
[2]School of Veterinary Medicine, University of California, Tulare 93274
[3]University of Chinese Academy of Sciences, Beijing 100049, P. R. China
[4]Agricultural Innovation Institute of Panama (IDIAP), City of Knowledge 07144, Panama
[5]Animal Resource Program, The Pennsylvania State University, University Park 16802
[6]Ajinomoto Co. Inc., Kawasaki, Japan 210-8681

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Histidine work at Penn State

- Observed a consistent apparent drop in plasma His with long-term feeding of low-CP diets
- His is unique among EAA: depots of labile His in muscle dipeptides and blood cholesterol
- Hypothesis: on low-CP diets, microbial protein is becoming an increasingly important source of AA for the cow
    - However, compared with Met, microbial protein is a poorer source of His

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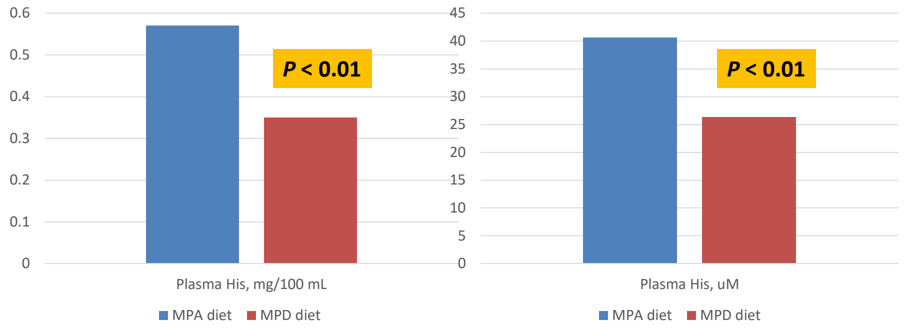
Lee et al., 2012; Giallongo et al., 2016

A couple of examples of the effect of dietary CP/MP on plasma His



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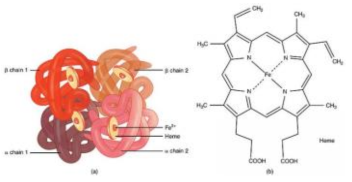
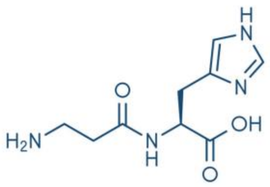
Endogenous sources of His



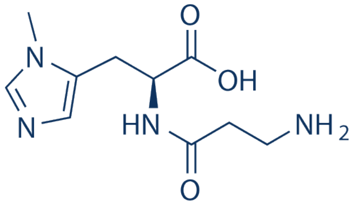
Hemoglobin

Giallongo et al., 2017:

- Blood hemoglobin = 380 g mHis
- Muscle carnosine & anserine = 270 g mHis
- These could supply mHis for about 7 wks (at approx. – 6 g mHis/d deficiency)



Carnosine



Anserine

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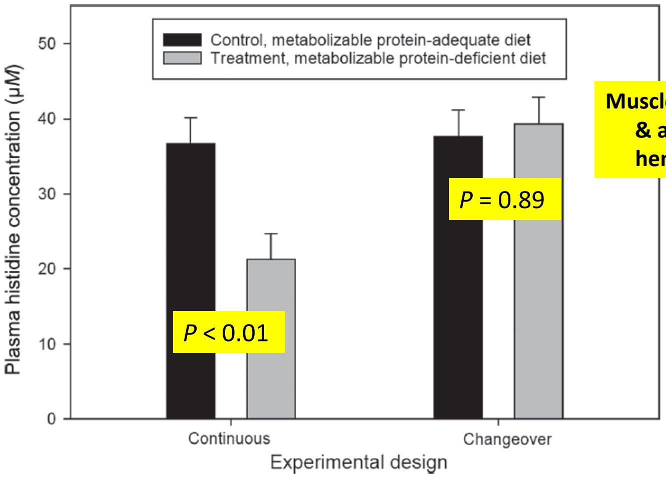
Hristov et al., 2019 (data from Lee et al., 2012, 2015)

Body reserves can hide temporary His deficiencies



$P < 0.01$

$P = 0.89$

Muscle carnosine & anserine, hemoglobin

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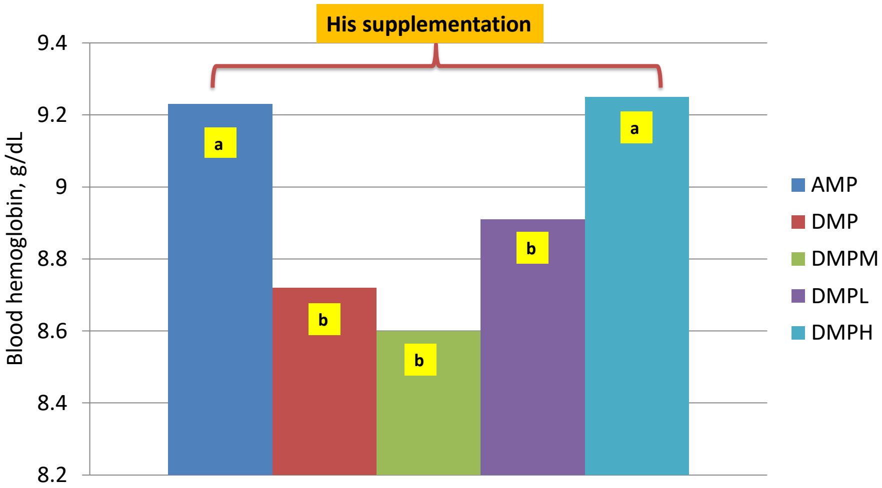
Giallongo et al., 2015

His and blood hemoglobin

His supplementation



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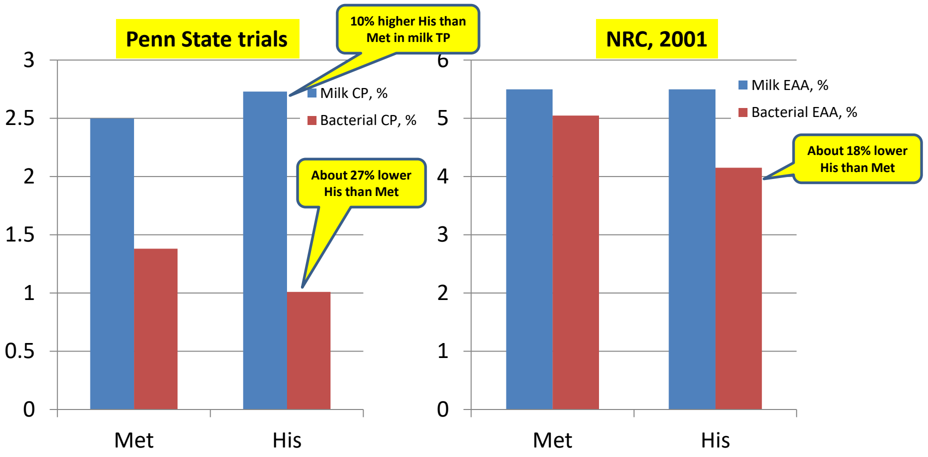
Met and His in milk protein vs. bacteria



10% higher His than Met in milk TP

About 27% lower His than Met

About 18% lower His than Met

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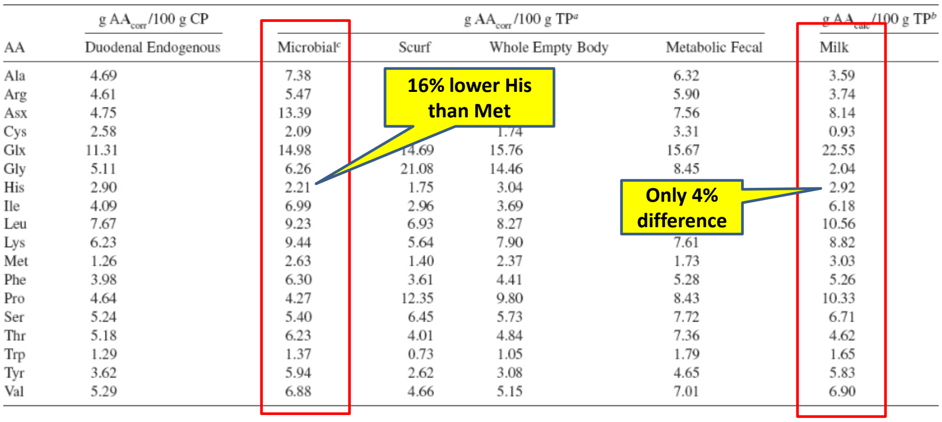
NASEM (2021) AA composition of microbial protein



	g AA$_{corr}$/100 g CP	g AA$_{corr}$/100 g TP^a				g AA$_{calc}$/100 g TP^b
AA	Duodenal Endogenous	Microbial^c	Scurf	Whole Empty Body	Metabolic Fecal	Milk
Ala	4.69	7.38	[illegible]	[illegible]	6.32	3.59
Arg	4.61	5.47	[illegible]	[illegible]	5.90	3.74
Asx	4.75	13.39	[illegible]	[illegible]	7.56	8.14
Cys	2.58	2.09	[illegible]	1.74	3.31	0.93
Glx	11.31	14.98	14.69	15.76	15.67	22.55
Gly	5.11	6.26	21.08	14.46	8.45	2.04
His	2.90	2.21	1.75	3.04	[illegible]	2.92
Ile	4.09	6.99	2.96	3.69	[illegible]	6.18
Leu	7.67	9.23	6.93	8.27	[illegible]	10.56
Lys	6.23	9.44	5.64	7.90	7.61	8.82
Met	1.26	2.63	1.40	2.37	1.73	3.03
Phe	3.98	6.30	3.61	4.41	5.28	5.26
Pro	4.64	4.27	12.35	9.80	8.43	10.33
Ser	5.24	5.40	6.45	5.73	7.72	6.71
Thr	5.18	6.23	4.01	4.84	7.36	4.62
Trp	1.29	1.37	0.73	1.05	1.79	1.65
Tyr	3.62	5.94	2.62	3.08	4.65	5.83
Val	5.29	6.88	4.66	5.15	7.01	6.90

16% lower His than Met

Only 4% difference

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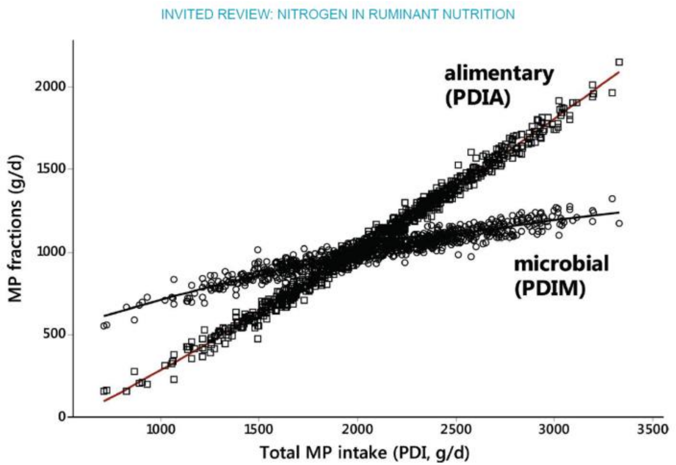
INRA data from Hristov et al., 2019

The relative contribution of microbial protein to the total MP supply is higher with low MP diets



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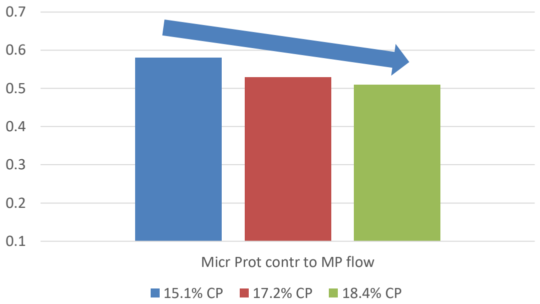
NASEM 2021 simulations

Mature, 700 kg BW Holstein cow, 100 DIM, 55 kg milk/d, 3.30% fat, 2.80% TP, 28 kg/d DMI

Diet CP, %	Proportion of microbial MP	Total mHis, g/d	mHis efficiency (target is 0.75)	N excretions, g/d
15.1	0.58	56	1.04	402
17.2	0.53	67	0.87	488
18.4	0.51	73	0.80	539



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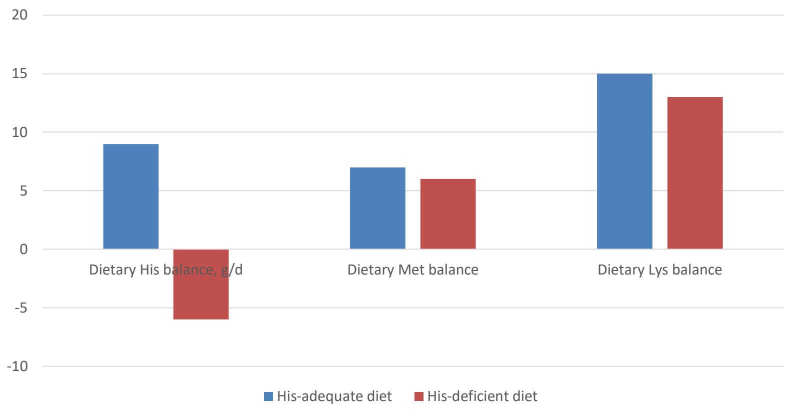
Histidine deficiency has a negative effect on lactational performance of dairy cows

F. Giallongo,* M. T. Harper,* J. Oh,* C. Parys,† I. Shinzato,‡ and A. N. Hristov*[1]
*Department of Animal Science, The Pennsylvania State University, University Park 16802
†Evonik Nutrition and Care GmbH, 63457 Hanau, Germany
‡Ajinomoto Co. Inc., Tokyo, Japan 104



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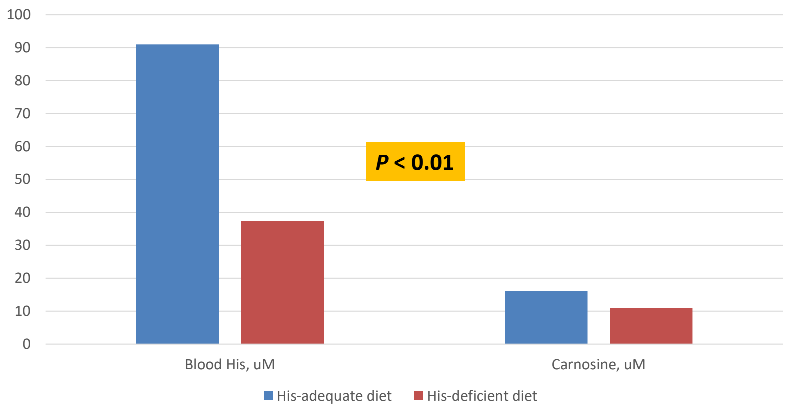

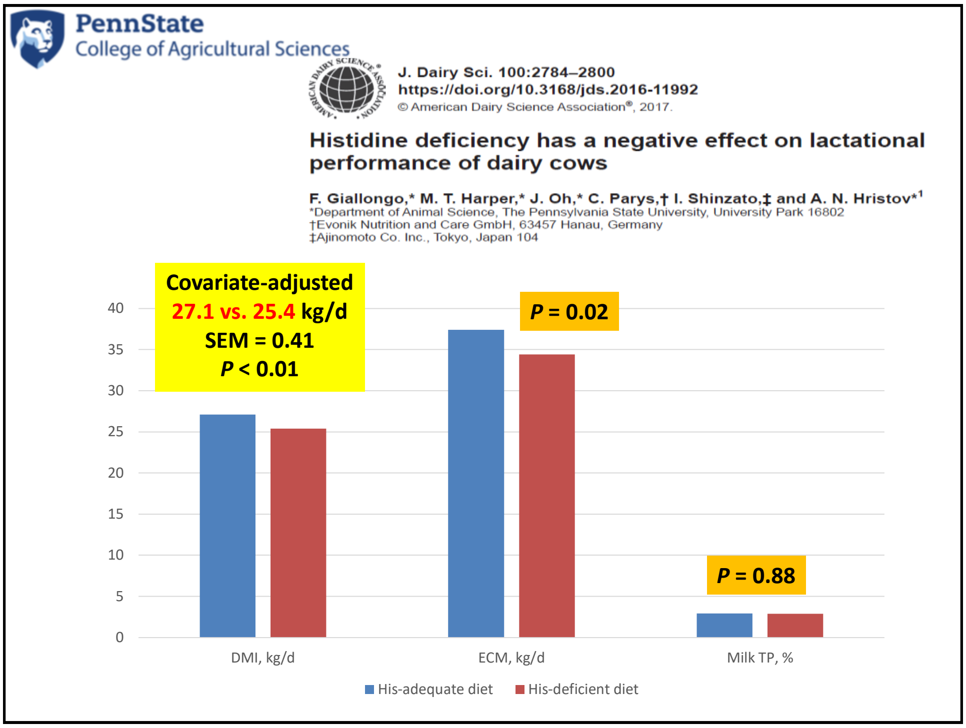

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‡Ajinomoto Co. Inc., Tokyo, Japan 104

Covariate-adjusted
27.1 vs. 25.4 kg/d
SEM = 0.41
***P* < 0.01**

***P* = 0.02**

***P* = 0.88**

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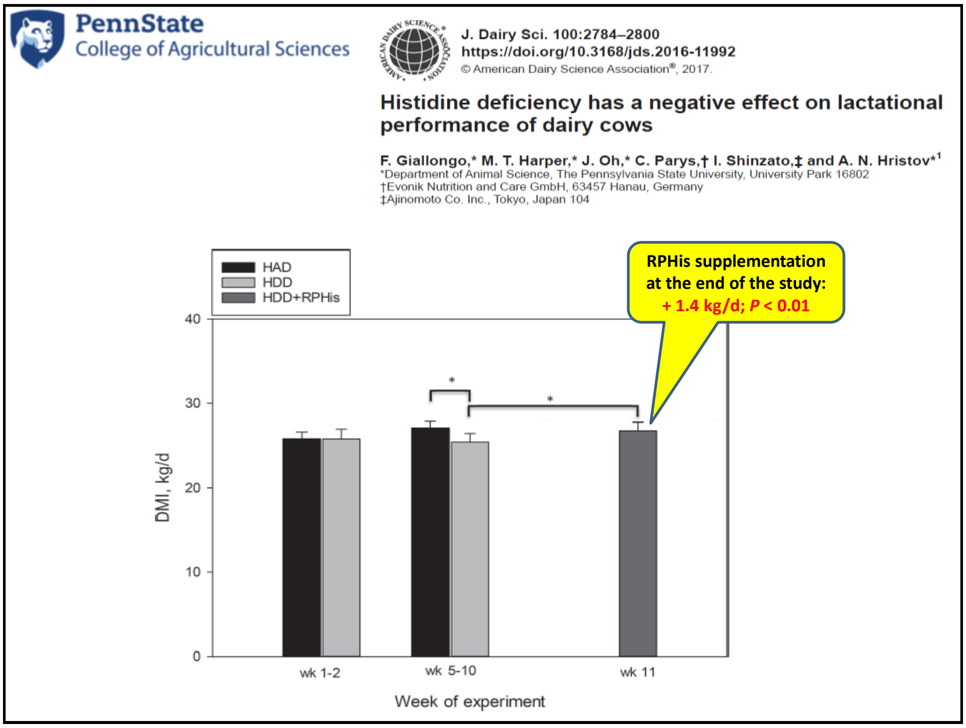

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‡Ajinomoto Co. Inc., Tokyo, Japan 104

RPHis supplementation at the end of the study:
+ 1.4 kg/d; *P* < 0.01

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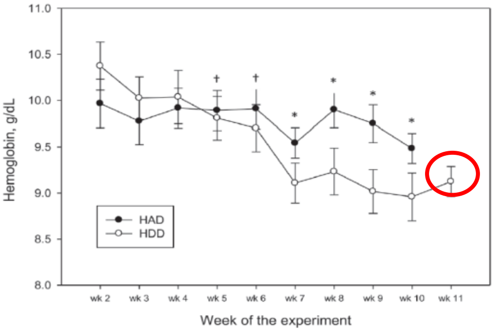
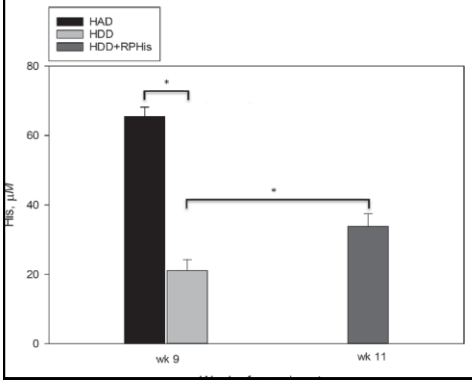
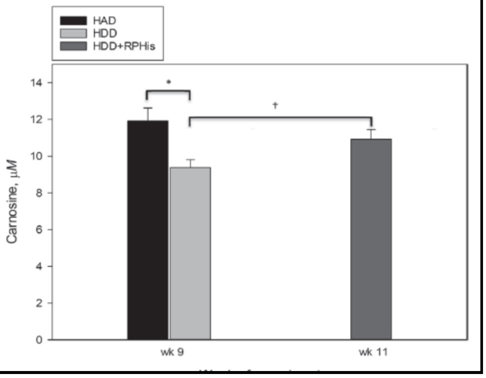
Giallongo et al., 2017

Blood hemoglobin, His, and carnosine as affected by His deficiency







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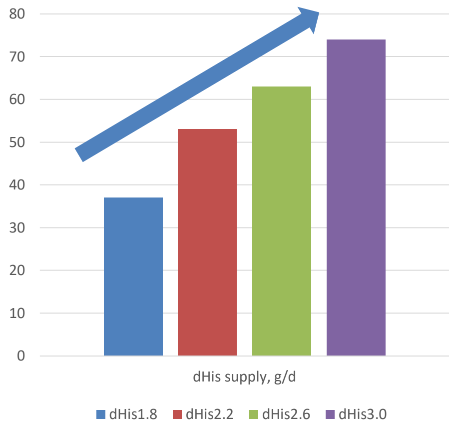
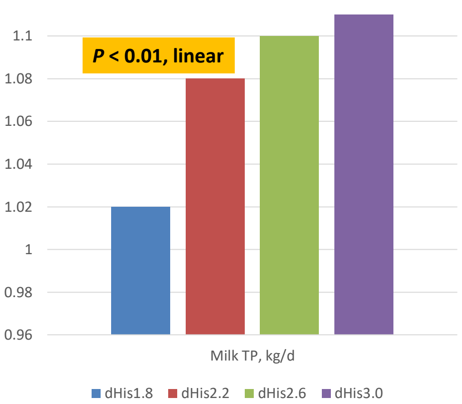
Histidine dose-response effects on lactational performance and plasma amino acid concentrations in lactating dairy cows: 2. Metabolizable protein-deficient diet

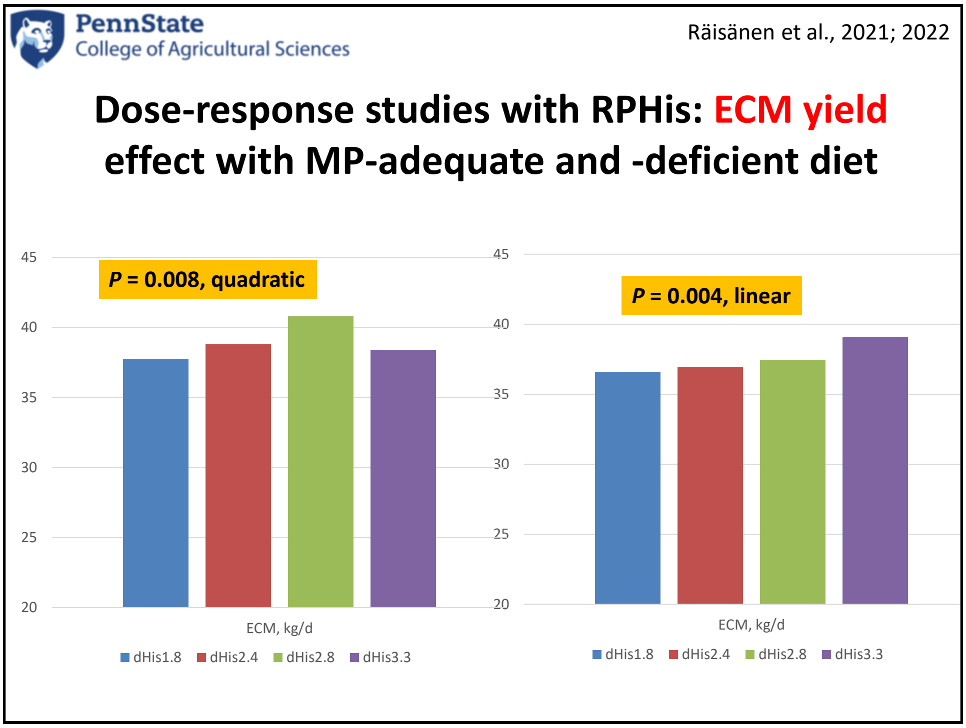
S. E. Räisänen,[1] C. F. A. Lage,[1,2] M. E. Fetter,[1] A. Melgar,[1,3] A. M. Pelaez,[1,4] H. A. Stefenoni,[1] D. E. Wasson,[1] S. F. Cueva,[1] X. Zhu,[1,5] M. Miura,[6] and A. N. Hristov[1]*
[1]Department of Animal Science, The Pennsylvania State University, University Park 16802
[2]School of Veterinary Medicine, University of California, Davis, Tulare 93274
[3]Agricultural Innovation Institute of Panama (IDIAP), City of Knowledge 07144, Panama
[4]Wageningen University and Research, PO Box 338, 6700 AH Wageningen, the Netherlands
[5]University of Chinese Academy of Sciences, Beijing 100049, P. R. China
[6]Ajinomoto Co. Inc., Kawasaki, Japan 210-8681

Lactational performance was optimized at dHis supply of 74 g/d (or 3.0% of MP)
No effect on MTP in the MPA diet trial

Linear increase in MY and FE, no effect on DMI




$P < 0.01$, linear



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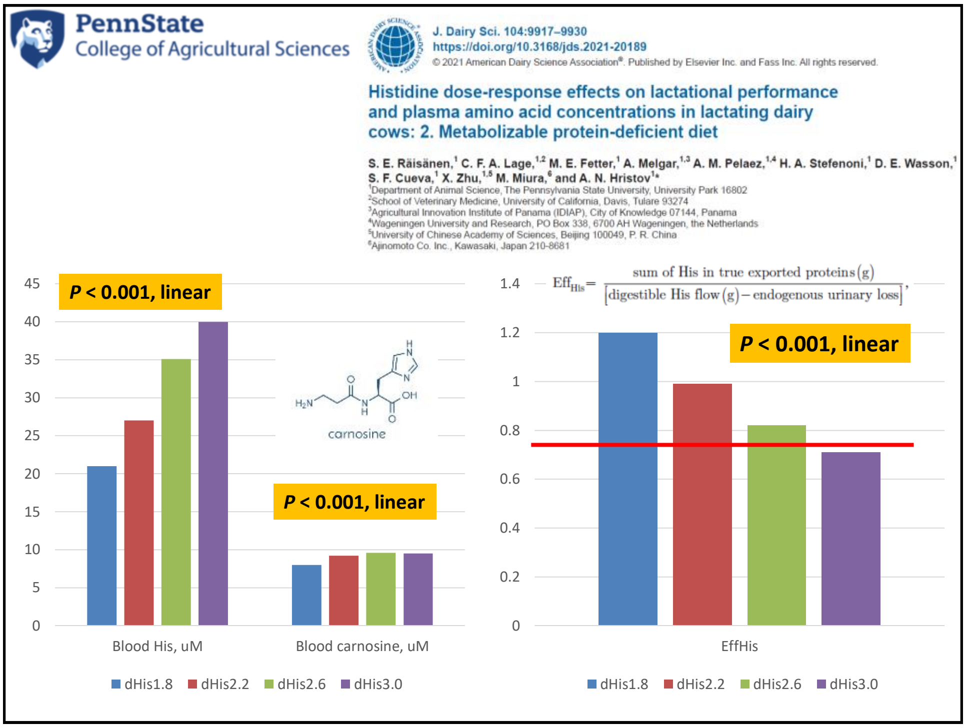
Räisänen et al., 2021; 2022

Dose-response studies with RPHis: ECM yield effect with MP-adequate and -deficient diet

$P = 0.008$, quadratic

$P = 0.004$, linear

39



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[6]Ajinomoto Co. Inc., Kawasaki, Japan 210-8681

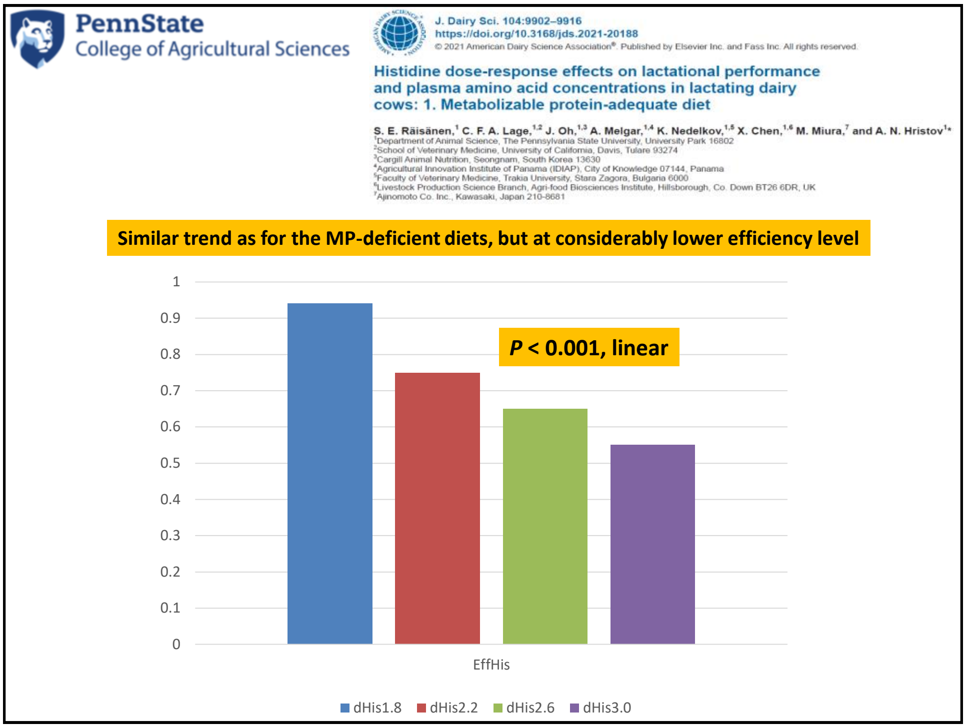
$$\mathrm{Eff}_{\mathrm{His}} = \frac{\text{sum of His in true exported proteins}\,(\mathrm{g})}{\left[\text{digestible His flow}\,(\mathrm{g}) - \text{endogenous urinary loss}\right]},$$

$P < 0.001$, linear

$P < 0.001$, linear

$P < 0.001$, linear

40



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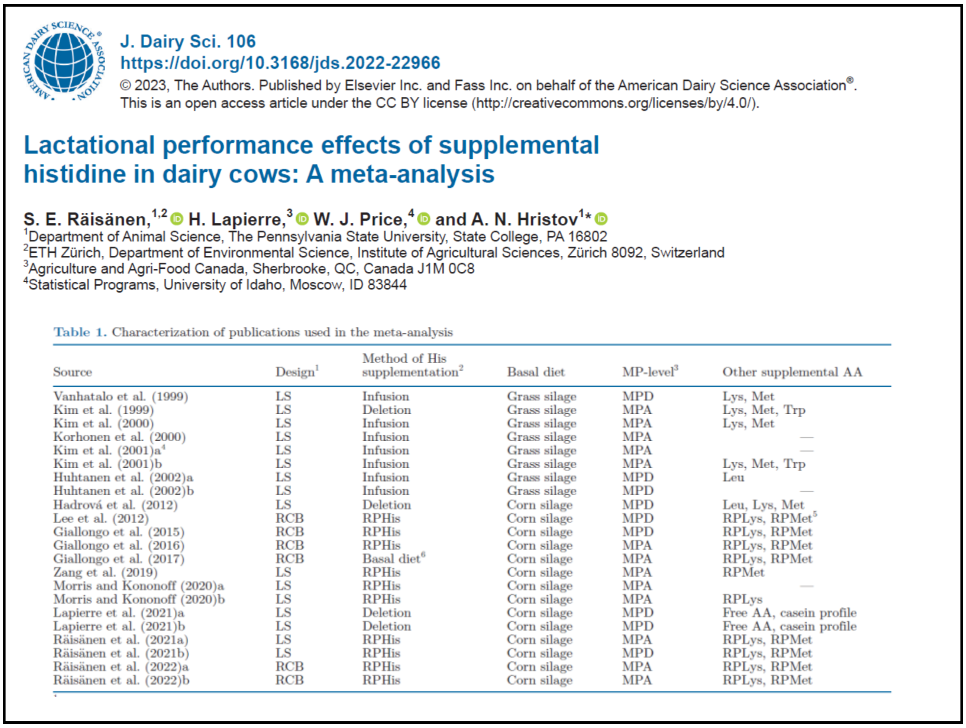
Histidine dose-response effects on lactational performance and plasma amino acid concentrations in lactating dairy cows: 1. Metabolizable protein-adequate diet

S. E. Räisänen,[1] C. F. A. Lage,[1,2] J. Oh,[1,3] A. Melgar,[1,4] K. Nedelkov,[1,5] X. Chen,[1,6] M. Miura,[7] and A. N. Hristov[1*]
[1]Department of Animal Science, The Pennsylvania State University, University Park 16802
[2]School of Veterinary Medicine, University of California, Davis, Tulare 93274
[3]Cargill Animal Nutrition, Seongnam, South Korea 13630
[4]Agricultural Innovation Institute of Panama (IDIAP), City of Knowledge 07144, Panama
[5]Faculty of Veterinary Medicine, Trakia University, Stara Zagora, Bulgaria 6000
[6]Livestock Production Science Branch, Agri-food Biosciences Institute, Hillsborough, Co. Down BT26 6DR, UK
[7]Ajinomoto Co. Inc., Kawasaki, Japan 210-8681

Similar trend as for the MP-deficient diets, but at considerably lower efficiency level



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Lactational performance effects of supplemental histidine in dairy cows: A meta-analysis

S. E. Räisänen,[1,2] H. Lapierre,[3] W. J. Price,[4] and A. N. Hristov[1*]
[1]Department of Animal Science, The Pennsylvania State University, State College, PA 16802
[2]ETH Zürich, Department of Environmental Science, Institute of Agricultural Sciences, Zürich 8092, Switzerland
[3]Agriculture and Agri-Food Canada, Sherbrooke, QC, Canada J1M 0C8
[4]Statistical Programs, University of Idaho, Moscow, ID 83844

Table 1. Characterization of publications used in the meta-analysis

Source	Design[1]	Method of His supplementation[2]	Basal diet	MP-level[3]	Other supplemental AA
Vanhatalo et al. (1999)	LS	Infusion	Grass silage	MPD	Lys, Met
Kim et al. (1999)	LS	Deletion	Grass silage	MPA	Lys, Met, Trp
Kim et al. (2000)	LS	Infusion	Grass silage	MPA	Lys, Met
Korhonen et al. (2000)	LS	Infusion	Grass silage	MPA	—
Kim et al. (2001)a[4]	LS	Infusion	Grass silage	MPA	—
Kim et al. (2001)b	LS	Infusion	Grass silage	MPA	Lys, Met, Trp
Huhtanen et al. (2002)a	LS	Infusion	Grass silage	MPD	Leu
Huhtanen et al. (2002)b	LS	Infusion	Grass silage	MPD	—
Hadrová et al. (2012)	LS	Deletion	Corn silage	MPD	Leu, Lys, Met
Lee et al. (2012)	RCB	RPHis	Corn silage	MPD	RPLys, RPMet[5]
Giallongo et al. (2015)	RCB	RPHis	Corn silage	MPD	RPLys, RPMet
Giallongo et al. (2016)	RCB	RPHis	Corn silage	MPA	RPLys, RPMet
Giallongo et al. (2017)	RCB	Basal diet[6]	Corn silage	MPA	RPLys, RPMet
Zang et al. (2019)	LS	RPHis	Corn silage	MPA	RPMet
Morris and Kononoff (2020)a	LS	RPHis	Corn silage	MPA	—
Morris and Kononoff (2020)b	LS	RPHis	Corn silage	MPA	RPLys
Lapierre et al. (2021)a	LS	Deletion	Corn silage	MPD	Free AA, casein profile
Lapierre et al. (2021)b	LS	Deletion	Corn silage	MPD	Free AA, casein profile
Räisänen et al. (2021a)	LS	RPHis	Corn silage	MPA	RPLys, RPMet
Räisänen et al. (2021b)	LS	RPHis	Corn silage	MPD	RPLys, RPMet
Räisänen et al. (2022)a	RCB	RPHis	Corn silage	MPA	RPLys, RPMet
Räisänen et al. (2022)b	RCB	RPHis	Corn silage	MPA	RPLys, RPMet

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[1]Department of Animal Science, The Pennsylvania State University, State College, PA 16802
[2]ETH Zürich, Department of Environmental Science, Institute of Agricultural Sciences, Zürich 8092, Switzerland
[3]Agriculture and Agri-Food Canada, Sherbrooke, QC, Canada J1M 0C8
[4]Statistical Programs, University of Idaho, Moscow, ID 83844

Table 4. Effect size[1] and heterogeneity for the effect of His supplementation on lactational performance of dairy cows

		Effect size and 95% CI					Heterogeneity	
Item	N[2]	Random	SE	Lower limit	Upper limit	*P*-value	Q-value[3]	*P*-value
DMI, kg/d	22	0.241	0.097	0.050	0.432	0.01	21.4	0.44
Milk yield, kg/d	22	0.888	0.192	0.512	1.26	<0.001	69.4	<0.001
ECM yield,[4] kg/d	14	0.187	0.115	−0.039	0.413	0.11	8.78	0.85
Milk true protein, %	22	0.246	0.104	0.041	0.450	0.02	23.9	0.30
Milk true protein, kg/d	22	0.674	0.147	0.386	0.962	<0.001	42.8	0.003
Milk fat, %	22	−0.427	0.119	−0.660	−0.195	<0.001	29.7	0.10
Milk fat, kg/d	22	−0.009	0.096	−0.197	0.178	0.92	12.6	0.92
Milk lactose, %	20	0.004	0.121	−0.234	0.241	0.97	27.1	0.10
Milk lactose, kg/d	20	0.425	0.101	0.227	0.623	<0.001	43.7	0.001
Plasma His, m*M*	22	1.81	0.251	1.39	2.37	<0.001	92.3	<0.001

[1]Computed as standard mean difference = raw mean difference of treatment and control means divided by the pooled SD of the means; values of <0.2, 0.2 to 0.7, and >0.7, were considered small, moderate, or large, respectively.

[2]Number of studies.

[3]Chi-squared (Q) test for heteroneity and variation among the study level.

[4]Six studies were excluded from the analysis due to lack of ECM data and respective SD in the publication.

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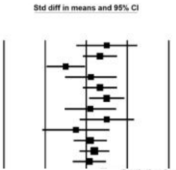
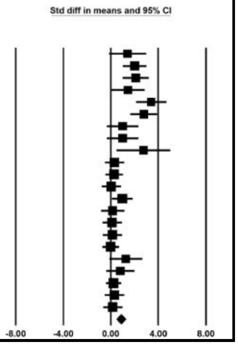
DMI

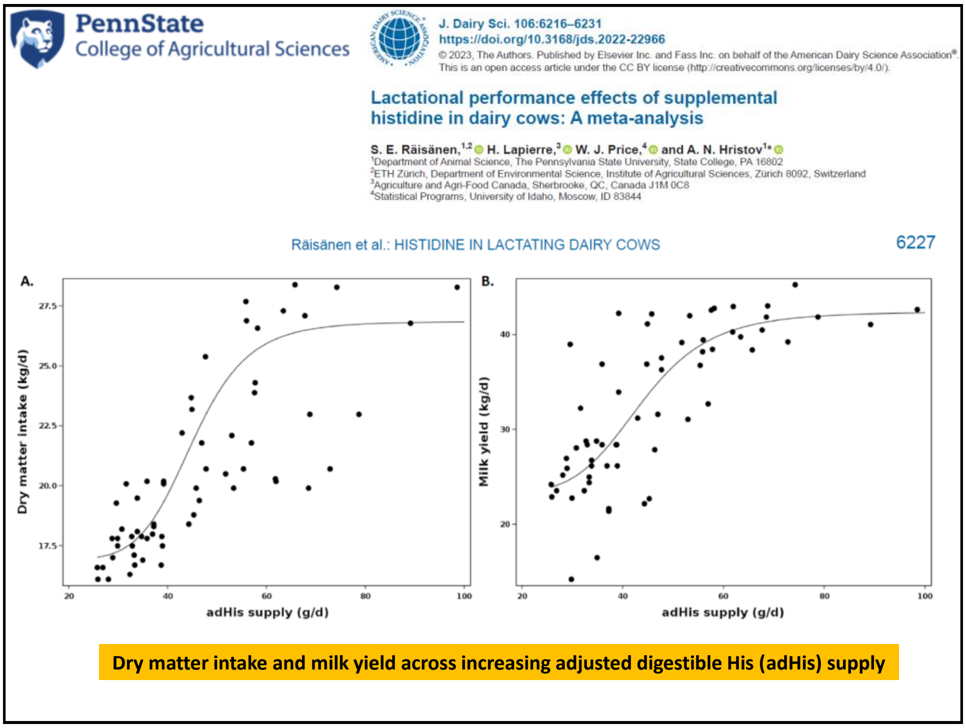
Study name	Statistics for each study						
	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Vanhatalo et al. (1999)	1.000	0.750	0.563	-0.470	2.470	1.333	0.182
Kim et al. (1999)	0.667	0.419	0.176	-0.155	1.489	1.589	0.112
Kim et al. (2000)	-1.000	0.474	0.225	-1.930	-0.070	-2.108	0.035
Korhonen et al. (2000)	0.222	0.634	0.402	-1.021	1.466	0.350	0.726
Kim et al. (2001)a	0.667	0.419	0.176	-0.155	1.489	1.589	0.112
Kim et al. (2001)b	1.000	0.433	0.188	0.151	1.849	2.309	0.021
Huhtanen et al. (2002)a	0.200	0.634	0.402	-1.043	1.443	0.315	0.752
Huhtanen et al. (2002)b	1.000	0.671	0.450	-0.315	2.315	1.491	0.136
Hadrova et al. (2012)	-0.500	0.829	0.688	-2.125	1.125	-0.603	0.546
Lee et al. (2012)	0.200	0.409	0.168	-0.602	1.002	0.489	0.625
Giallongo et al. (2015)	0.395	0.369	0.136	-0.327	1.118	1.072	0.284
Giallongo et al. (2016)	0.149	0.409	0.167	-0.652	0.950	0.364	0.716
Giallongo et al. (2017)	0.850	0.426	0.182	0.014	1.686		
Zang et al. (2019)	-0.200	0.501	0.251	-1.182	0.782		
Morris and Kononoff (2020)a	0.000	0.408	0.167	-0.800	0.800		
Morris and Kononoff (2020)b	0.172	0.409	0.167	-0.629	0.974		
Räisänen et al. (2021a)	-0.158	0.354	0.125	-0.852	0.536		
Lapierre et al. (2021)a	0.333	0.637	0.406	-0.915	1.582		
Lapierre et al. (2021)b	0.778	0.599	0.359	-0.396	1.951		
Räisänen et al. (2021b)	0.043	0.316	0.100	-0.576	0.663		
Räisänen et al. (2022)a	0.145	0.409	0.167	-0.656	0.946		
Räisänen et al. (2022)b	0.014	0.408	0.167	-0.786	0.815		
Pooled	0.241	0.097	0.009	0.050	0.432		



Milk yield

Study name	Statistics for each study						
	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Vanhatalo et al. (1999)	1.400	0.789	0.623	-0.146	2.946	1.774	0.076
Kim et al. (1999)	2.000	0.500	0.250	1.020	2.980	4.000	0.000
Kim et al. (2000)	2.091	0.556	0.309	1.001	3.181	3.760	0.000
Korhonen et al. (2000)	1.444	0.710	0.504	0.053	2.836	2.034	0.042
Kim et al. (2001)a	3.400	0.638	0.408	2.149	4.651	5.326	0.000
Kim et al. (2001)b	2.778	0.572	0.327	1.656	3.899	4.855	0.000
Huhtanen et al. (2002)a	1.000	0.671	0.450	-0.315	2.315	1.491	0.136
Huhtanen et al. (2002)b	1.000	0.671	0.450	-0.315	2.315	1.491	0.136
Hadrova et al. (2012)	2.750	1.139	1.297	0.518	4.982	2.415	0.016
Lee et al. (2012)	0.314	0.411	0.169	-0.491	1.119	0.764	0.445
Giallongo et al. (2015)	0.275	0.367	0.135	-0.444	0.994	0.749	0.454
Giallongo et al. (2016)	0.034	0.408	0.167	-0.766	0.834	0.083	0.934
Giallongo et al. (2017)	0.967	0.431	0.186	0.121	1.812	2.241	0.025
Zang et al. (2019)	0.158	0.501	0.251	-0.824	1.139	0.315	0.753
Morris and Kononoff (2020)a	0.113	0.409	0.167	-0.688	0.913	0.276	0.783
Morris and Kononoff (2020)b	0.141	0.409	0.167	-0.660	0.942	0.345	0.730
Räisänen et al. (2021a)	-0.009	0.354	0.125	-0.702	0.684	-0.026	0.979
Lapierre et al. (2021)a	1.259	0.692	0.479	-0.098	2.616	1.819	0.069
Lapierre et al. (2021)b	0.805	0.600	0.360	-0.372	1.981	1.341	0.180
Räisänen et al. (2021b)	0.231	0.317	0.101	-0.391	0.853	0.727	0.467
Räisänen et al. (2022)a	0.309	0.411	0.169	-0.496	1.113	0.751	0.453
Räisänen et al. (2022)b	0.170	0.409	0.167	-0.631	0.972	0.416	0.677
Pooled	0.888	0.192	0.037	0.512	1.264	4.626	0.000





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Lactational performance effects of supplemental histidine in dairy cows: A meta-analysis

S. E. Räisänen,[1,2] **H. Lapierre,**[3] **W. J. Price,**[4] **and A. N. Hristov**[1*]
[1]Department of Animal Science, The Pennsylvania State University, State College, PA 16802
[2]ETH Zürich, Department of Environmental Science, Institute of Agricultural Sciences, Zürich 8092, Switzerland
[3]Agriculture and Agri-Food Canada, Sherbrooke, QC, Canada J1M 0C8
[4]Statistical Programs, University of Idaho, Moscow, ID 83844

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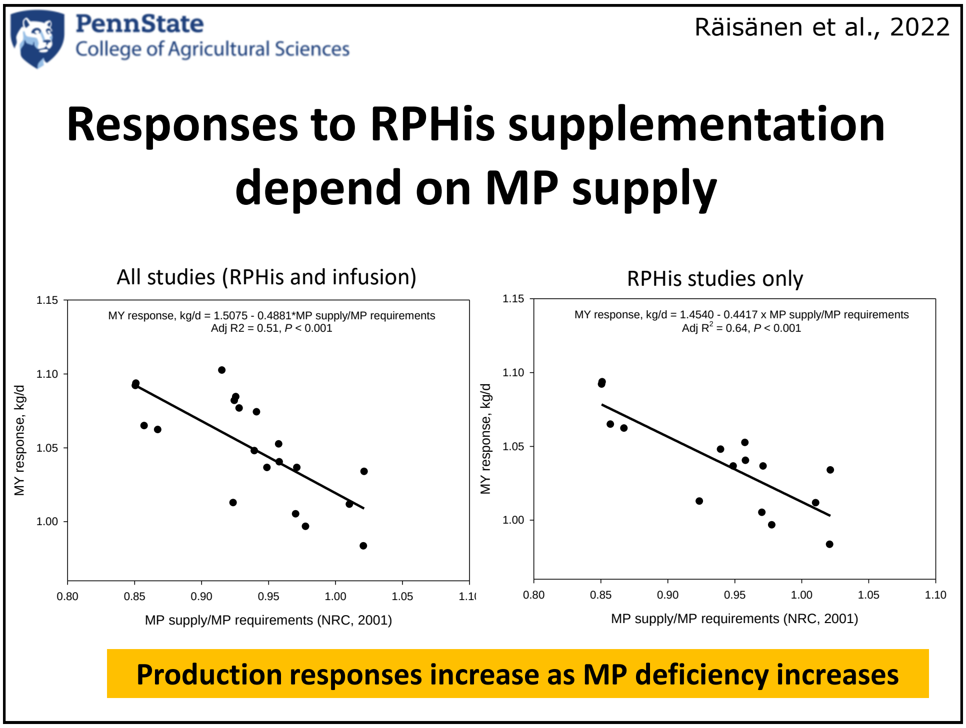
Dry matter intake and milk yield across increasing adjusted digestible His (adHis) supply



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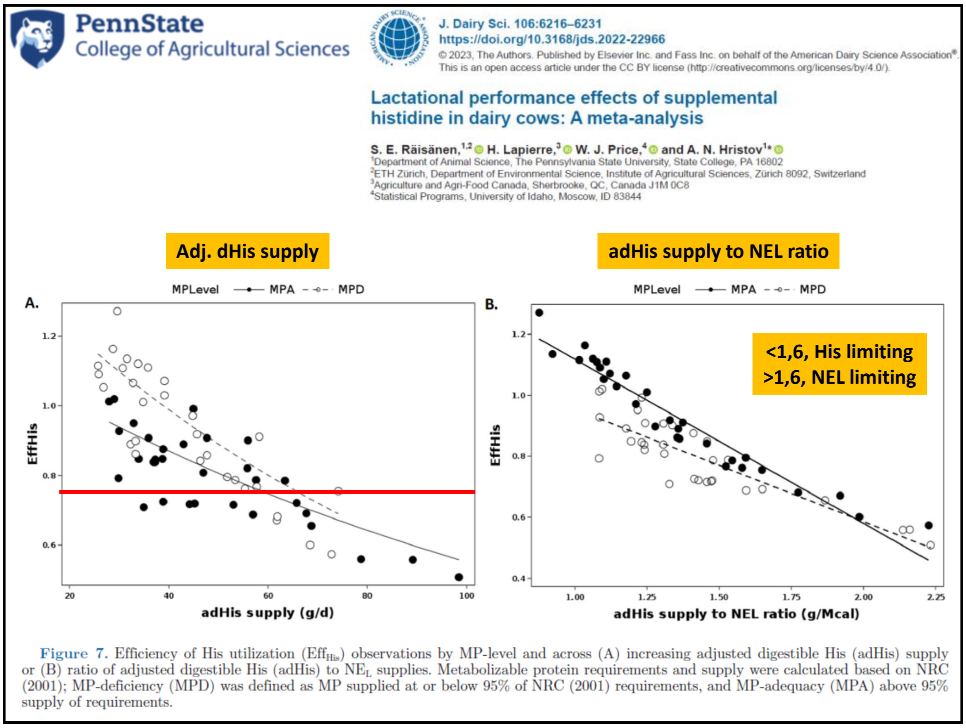
Räisänen et al., 2022

Responses to RPHis supplementation depend on MP supply

All studies (RPHis and infusion)

RPHis studies only

Production responses increase as MP deficiency increases



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Lactational performance effects of supplemental histidine in dairy cows: A meta-analysis

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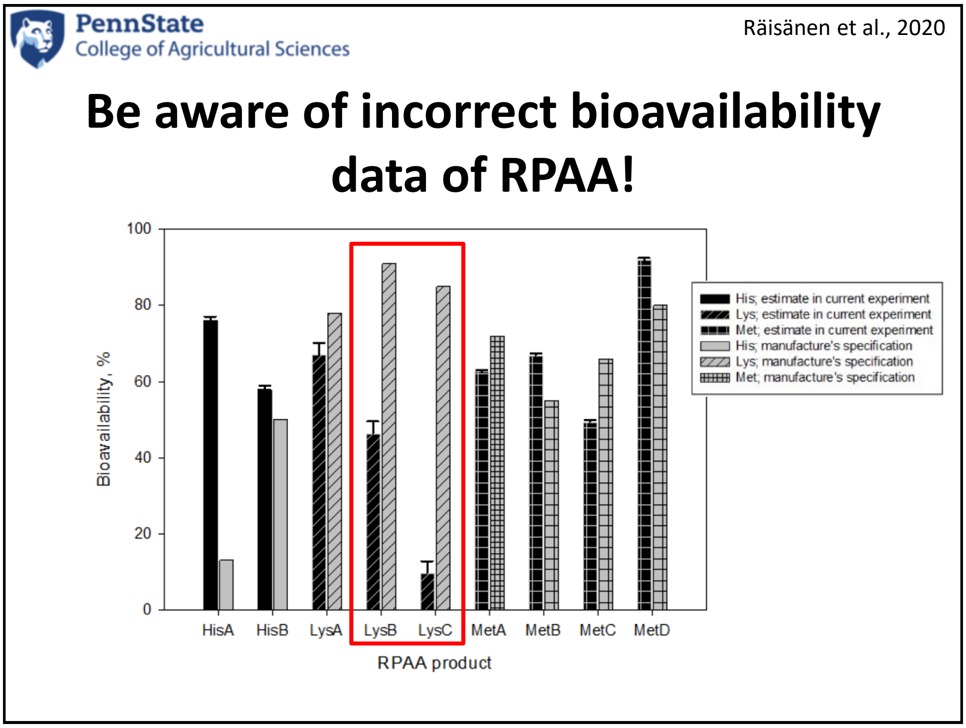
Adj. dHis supply

adHis supply to NEL ratio

<1,6, His limiting
>1,6, NEL limiting

Figure 7. Efficiency of His utilization (Eff_{His}) observations by MP-level and across (A) increasing adjusted digestible His (adHis) supply or (B) ratio of adjusted digestible His (adHis) to NE_{L} supplies. Metabolizable protein requirements and supply were calculated based on NRC (2001); MP-deficiency (MPD) was defined as MP supplied at or below 95% of NRC (2001) requirements, and MP-adequacy (MPA) above 95% supply of requirements.



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Räisänen et al., 2020

Be aware of incorrect bioavailability data of RPAA!

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Take-home message

- Dietary **protein intake is the most important factor determining nitrogen efficiency**, urinary nitrogen losses, and consequently, nitrate leaching and ammonia and nitrous oxide emissions from dairy cow manure
- Earlier and more recently studies with corn silage-based diets conducted at Penn State indicate that His may be a limiting AA in dairy cow **fed low-protein (< 16% CP) diets**
  - Long-term trials showed that **supplementation of such diets with rumen-protected His increased or tended to increase milk yield and milk protein percent and yield, partially through increasing DMI**
  - **Our data suggest dHis recommendations at around 3.0% of MP, or 70-74 g/d**
  - **Watch for false bioavailability data**
  - **Order and degree of AA limitation will likely depend on EAA profile of RUP**
- The effects of **low-protein, high-starch diets on enteric methane emission** and overall carbon footprint of milk needs to be further examined

QUESTIONS?