ReaShure®

# ReaShure Tool Kit

ReaShure® *Precision Release Choline*

TABLE OF CONTENTS




**For more Information Contact:**

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**anh@balchem.com**
**www.balchem.com**


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ReaShure®

Precision Release Choline

# ESSENTIAL TRANSITION NUTRITION

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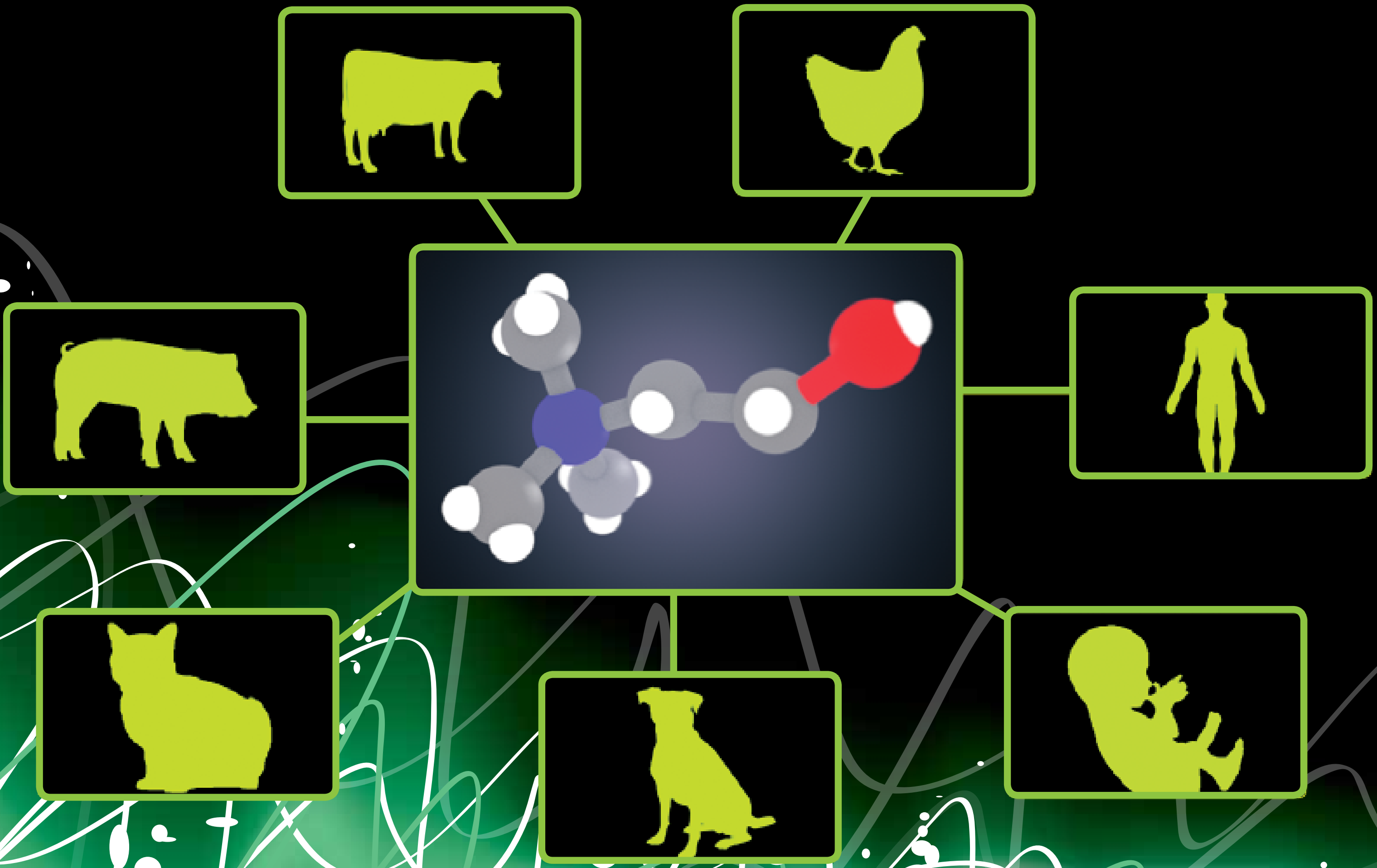
# CHOLINE
## ESSENTIAL FOR LIFE

Choline is essential for growth and health of all animals and humans. It is a biochemical building block, and precursor to numerous compounds necessary to support life.

In dairy cattle, choline is required to help the liver process and metabolize fat, especially during the critical transition period. A healthy and properly functioning liver can help cows transition more smoothly, creating a faster and more productive start to their lactation.

Every dairy cow is deficient in choline because dietary choline is degraded by rumen microorganisms and her body can not make enough to meet requirements. While a cow may consume choline in her diet, very little naturally escapes the rumen for absorption in the small intestine.



# ReaShure®

Precision Release Choline

## THE KEY TO A SMOOTH TRANSITION AND FASTER START

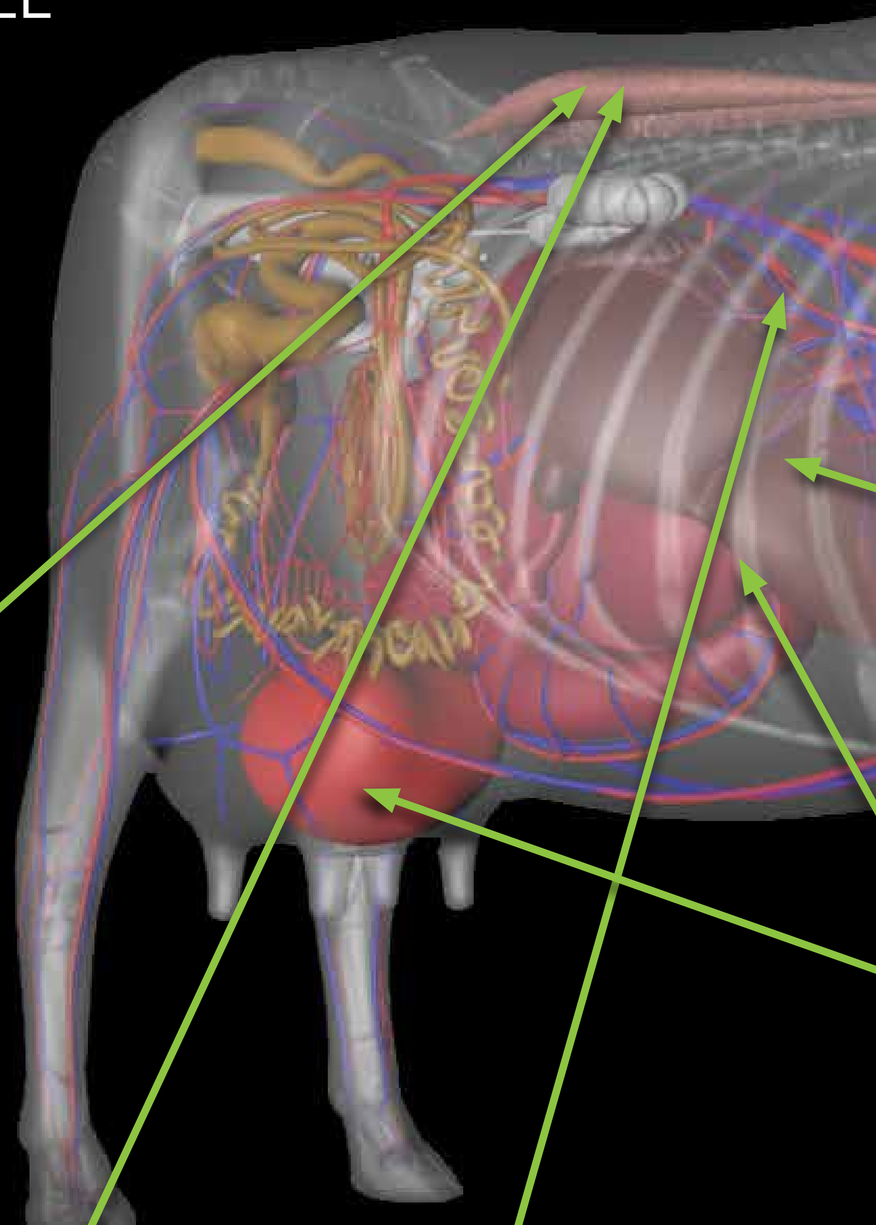
ReaShure® *Precision Release Choline* is encapsulated using a state-of-the-art process to protect the choline from degradation in the rumen. Feeding ReaShure is a proven way to meet the transition dairy cow's dietary choline requirements during the important transition period. By protecting choline from rumen degradation, it is available in the small intestine to support these critical processes.

- **Support Fat Metabolism - Cows experience hormonal changes and negative energy balance around calving time which causes fat to be mobilized from body stores. Choline is essential for effective fat transport out of the liver.**
- **Support Milk Production and Milk Fat Synthesis - The cow's liver uses choline to package the mobilized fat into very low density lipoproteins (VLDL) which are then transported to the mammary gland and used as a fuel source for synthesizing milk and milk fat.**
- **Reduce Metabolic Disorders - A healthy functioning liver supports improvements in clinical and subclinical transition-related disorders such as ketosis, metritis, displaced abomasums and mastitis, reducing treatments costs, death loss and involuntary culling.**

# REAL SCIENCE

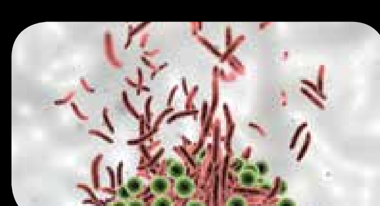
## CHOLINE'S CRITICAL ROLE

During transition, the cow's body enters an intense period of change and adjustment – preparing to support milk production. Choline is a key nutrient for packaging and exporting fat from the liver – part of the normal biology of "all" transition cows.

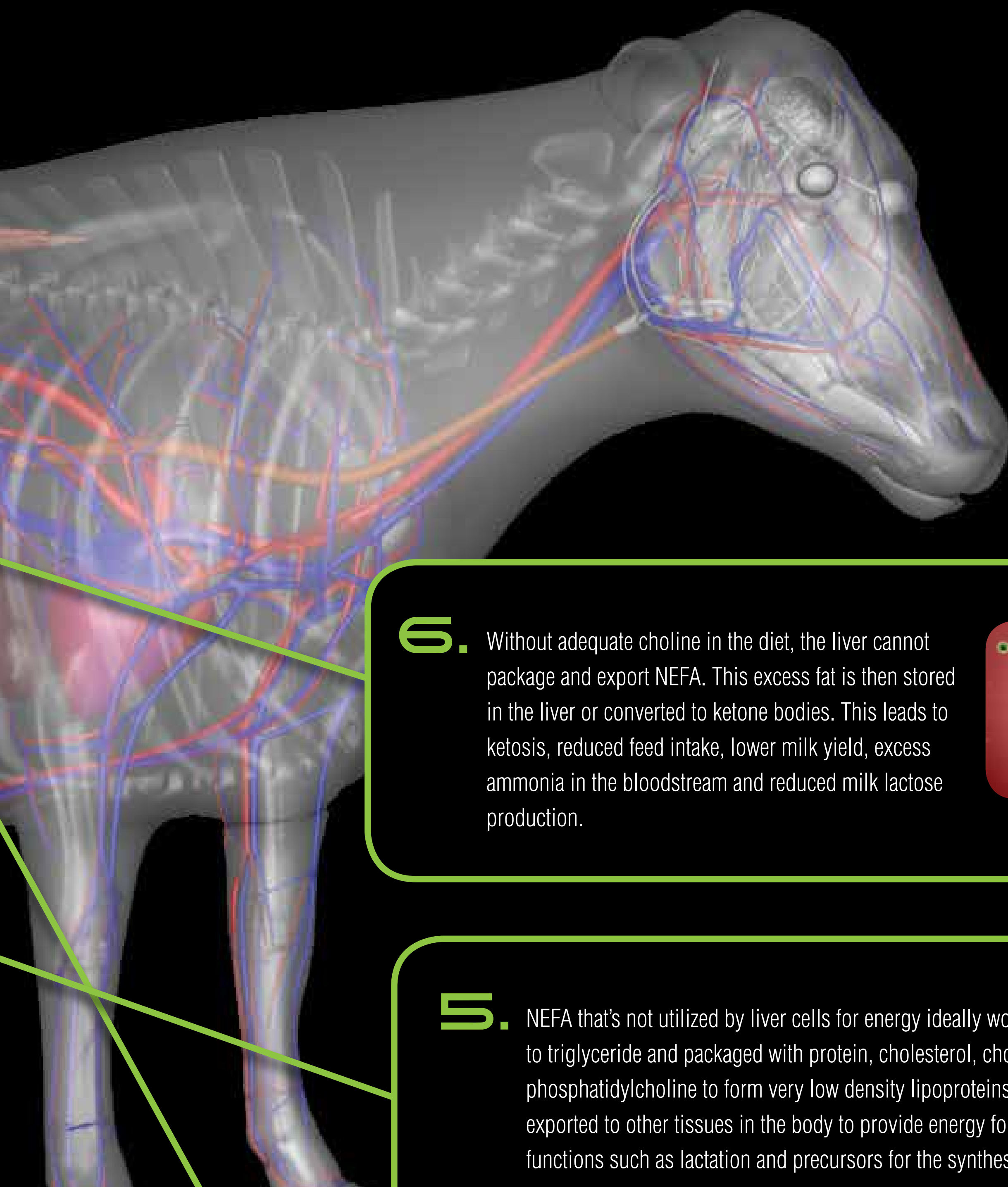


**1.** At calving, hormonal changes trigger an intense period of fat mobilization from body stores to meet the increased energy demand for milk production.

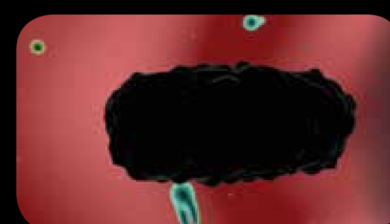
**2.** Hormones stimulate the hydrolysis of triglycerides into glycerol and fatty acids, commonly referred to as NEFA.



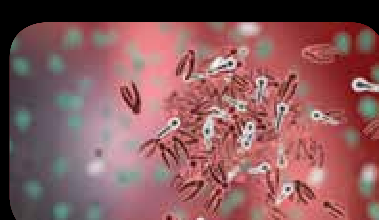
**3.** Blood NEFA concentrations surge and fatty acid uptake by the liver may increase 10-15-fold.

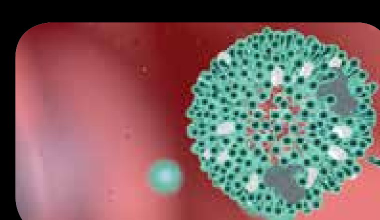


**6.** Without adequate choline in the diet, the liver cannot package and export NEFA. This excess fat is then stored in the liver or converted to ketone bodies. This leads to ketosis, reduced feed intake, lower milk yield, excess ammonia in the bloodstream and reduced milk lactose production.



**5.** NEFA that's not utilized by liver cells for energy ideally would be converted to triglyceride and packaged with protein, cholesterol, cholesterol ester, and phosphatidylcholine to form very low density lipoproteins (VLDL). VLDL can be exported to other tissues in the body to provide energy for important metabolic functions such as lactation and precursors for the synthesis of milk fat.





**4.** The liver's first priority is to oxidize NEFA completely to obtain energy for liver cell function.

# REAL RESULTS

ReaShure® *Precision Release Choline* has been extensively tested for more than a decade. This means we have an impressive body of data - University data, on-farm data, composite summary data. No matter how you slice it, ReaShure helps get cows through the difficult transition period and off to a quick start – the key to a successful lactation.

Research from the University of California-Davis measured changes in health disorders when animals were fed ReaShure. The potential economic impact of those differences was calculated using disease costs presented in a 2009 paper by Charles Guard DVM, PhD.

*Increased DMI by 6%*

**Economic Impact of Feeding ReaShure® *Precision Release Choline***

**Lima et al., 2012**

| | Control | ReaShure | P value | Income Difference $/cow |
|---|---|---|---|---|
| Improved 3.5% FCM Production, lb/h/d (kg/h/d) | 94.4 (42.8) | 98.3 (44.6) | 0.04 | $13.75[1] |
| **Reduced Health Disorders - Total** | 57.1% | 38.4% | 0.001 | $48.41[2] |
| *Retained Placenta* | 11.2% | 10.1% | | |
| *Metritis* | 11.3% | 7.9% | | |
| *Clinical ketosis* | 11.3% | 4.0% | | |
| *Displaced Abomasums* | 4.5% | 2.3% | | |
| *Mastitis* | 22.5% | 14.8% | | |
| Reduced Mortality | 7.1% | 4.5% | 0.27 | |
| Improved Dry Matter Intake, lb/h/d (kg/h/d) | 49.8 (22.6) | 52.7 (23.9) | 0.1 | $-9.01[3] |
| Grand Total | | | | **$53.15** |
| ReaShure Investment | | | | **$13.88[4]** |

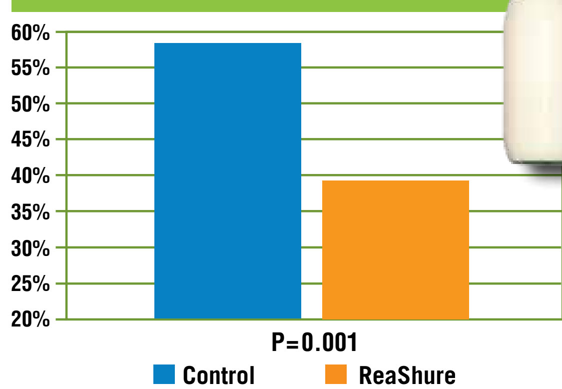
[1] $0.165/lb - All Milk 2015 Forecast
calculations made using 21 DIM to reflect the post-parturition recommended feeding period for ReaShure

[2] Guard C. 2009. CVC Kansas City Proceedings

[3] $14.97/cwt (USDA Milk Cost of Production report, average of Oct/Nov 2014)

[4] ReaShure at $2.50/lb fed for 42 days

**Differences in Health Disorders[1]**




[1] Includes retained placenta, metritis, ketosis and displacement of abomasum.

Source: F.S. Lima, J.E.P. Santos, M.F. Sa Filho, and J. Garrett, 2007

*13 university trials showed a mean increase of 4.9 lbs. milk/day*

ReaShure®
Precision Release Choline

NitroShure™
Precision Release Nitrogen

NiaShure™
Precision Release Niacin

VitaShure®-C
Precision Release Vitamin C

AminoShure®-M
Precision Release Methionine

AminoShure®-L
Precision Release Lysine

KeyShure®
Chelated Minerals

To learn more about ReaShure and its impact on transition cow physiology, view ReaShure – The Movie at **www.youtube.com/user/BalchemANH.**

**View ReaShure – The Movie**

For more ways to improve transition management, visit **www.transitioncow.net**. You'll find the summaries of the newest research, blog posts from transition nutrition and management experts and tools to help get your transition cows off to a smoother, faster start.

**Visit transitioncow.net**

To learn more about the complete portfolio of encapsulated nutrients and chelated minerals from Balchem, visit **anh.balchem.com**.

**Visit anh.balchem.com**

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BALCHEM

# THIS IS BALCHEM

Balchem is a science-driven nutrition company dedicated to the health and wellness of both humans and animals. Through nutrition innovations and manufacturing advances, Balchem is leading the way to a healthier and more sustainable world.

Built over the last 50 years, Balchem employs over 1,000 people worldwide across four business segments: Human Nutrition & Health; Animal Nutrition & Health; Specialty Products; and Industrial Products.

### Animal Nutrition & Health

Applying proven science and industry-leading technologies to meet the nutritional needs of animals, providing for greater health and performance.

### Human Nutrition & Health

Enhancing your dining pleasure through unique sensory experiences and delivering high quality nutrients that bring living to life.

### Industrial Products

Supplying environmentally friendly clay stabilizers to the oil field industry, reducing the amount of pollutants used in wells to ensure a cleaner, safer environment.

### Specialty Products

Providing the industry with technologies to sterilize items as diverse as medical devices and food items, ridding them of bacteria, fungi and insects that can cause health problems and complications.

Balchem Corporation is a publicly traded company listed on the NASDAQ Global Market under the symbol "BCPC." Our Corporate headquarters are located in New Hampton, New York, with manufacturing facilities located throughout the United States and in Marano Ticino, Italy.

# THIS IS ANIMAL NUTRITION & HEALTH

**RUMINANT**

ReaShure®
Precision Release Choline

AminoShure®-M
Precision Release Methionine

AminoShure®-L
Precision Release Lysine

NiaShure™
Precision Release Niacin

NitroShure™
Precision Release Nitrogen

VitaShure®-C
Precision Release Vitamin C

KeyShure®
Precision Release Minerals

**MONOGASTRIC**

Choline

KeyShure®
Precision Release Minerals

AMASIL®
Formic Acid

**COMPANION ANIMALS**

PetShure®
TURNING IMAGINATION INTO REALITY

POROSITY & TEXTURE MANAGEMENT

pH CONTROL SYSTEMS

STRUCTURING & FORMING TECHNOLOGIES

CHOLINE NON-GRAIN, NON-GMO

Balchem Animal Nutrition and Health is the global leader in choline production and encapsulation technology. With a growing portfolio of nutrition products and a dedication to innovation and industry sustainability, Balchem is leading the charge to meet the nutritional needs of ruminants, monogastrics and companion animals.

## WE ARE:

### Real People

With a passion for animal nutrition, we are intense advocates for our customers and the animals they feed. You can count on us to provide honest, candid advice to address your toughest challenges.

### Real Science

Balchem delivers proven science backed by years of success. Our products are some of the most extensively researched in the industry, further supported by documented on-farm results.

### Real Results

In the end, it all comes down to results. We deliver real results you can count on, results that exceed your expectations and deliver value to your customers and your bottom line.

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SALES MATERIALS

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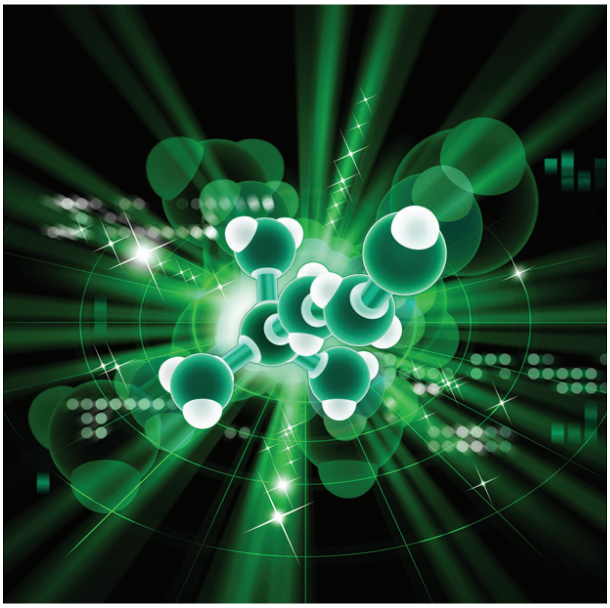
# ReaShure®

## Precision Release Choline



**ReaShure®** *Precision Release Choline* is an encapsulated choline product that protects the choline from rumen degradation and delivers it to the small intestine where it is absorbed. Choline is essential for the health of animals and humans because it's a biochemical building block and precursor to numerous compounds necessary to support life.

**Product Information:**
Content – 28.8% Choline Chloride

**Application:**
Feed to dairy animals during the transition period to meet their choline requirements. Choline is a required nutrient during the transition period used to help the liver process and deliver fat to the mammary gland.

**Ingredients:**
Fats, choline chloride and corn cob carrier

**Feeding recommendation:**
Dairy cows – 60 grams/head/day
Small Ruminants – 7 grams/head/day

For maximum benefit, begin feeding ReaShure 21 days before parturition and continue until 21 days after parturition. If grouping systems restrict the complete implementation of this feeding regime; partial benefits can be achieved by feeding ReaShure only during the pre-parturition or post-parturition periods.

**Packaging:**
25.0 kg (55.1 lb.) poly-lined bags
11.3 kg (25.0 lb.) poly-lined bags

**Availability**
ReaShure is available through most animal feed outlets. To find a local supply of ReaShure, see contact information on reverse side.

REASHURE® PRECISION RELEASE CHOLINE

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For more information, just snap the QR code or enter the url below.

- anh.balchem.com/anh/reashure
- Transitioncow.net
- ReaShure – the Movie www.youtube.com/user/BalchemANH.

## Balchem

For more than 40 years, Balchem has perfected the art of delivering nutrients to specific locations under many different environmental conditions. Today, Balchem's technologies protect more than 140 different products across human, animal and industrial applications. Protect your entire nutrient investment with Balchem.

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## Benefits:

ReaShure® *Precision Release Choline* is encapsulated using a state-of-the-art process, to protect the choline from degradation in the rumen. Feeding ReaShure is a proven way to meet the dietary choline requirements during the important transition period. By protecting choline from rumen degradation, it is available in the small intestine to support these critical processes.

- **Support Fat Metabolism** – Dairy animals experience hormonal changes and negative energy balance around calving time which causes fat to be mobilized from body stores. Choline is essential for effective fat transport out of the liver.
- **Support Milk Production and Milk Fat Synthesis** – The cow's liver uses choline to package the mobilized fat into very low density lipoproteins (VLDL) which are then transported to the mammary gland and either used as a fuel source for synthesizing milk and milk fat.
- **Reduce Metabolic Disorders** – A healthy, functioning liver supports improvements in clinical and subclinical transition-related disorders such as ketosis, metritis, displaced abomasums and mastitis.

## Economics:

Keeping dairy animals healthy during the critical transition period will save money on treatment costs, replacement animals, and lost milk. A smoother start will have a lasting economic impact on the entire lactation.

ReaShure® *Precision Release Choline* is proven to help dairy animals transition more smoothly, reducing the risk of metabolic disorders, supporting higher milk production, reproductive efficiency and overall animal health.

## Contact Information:

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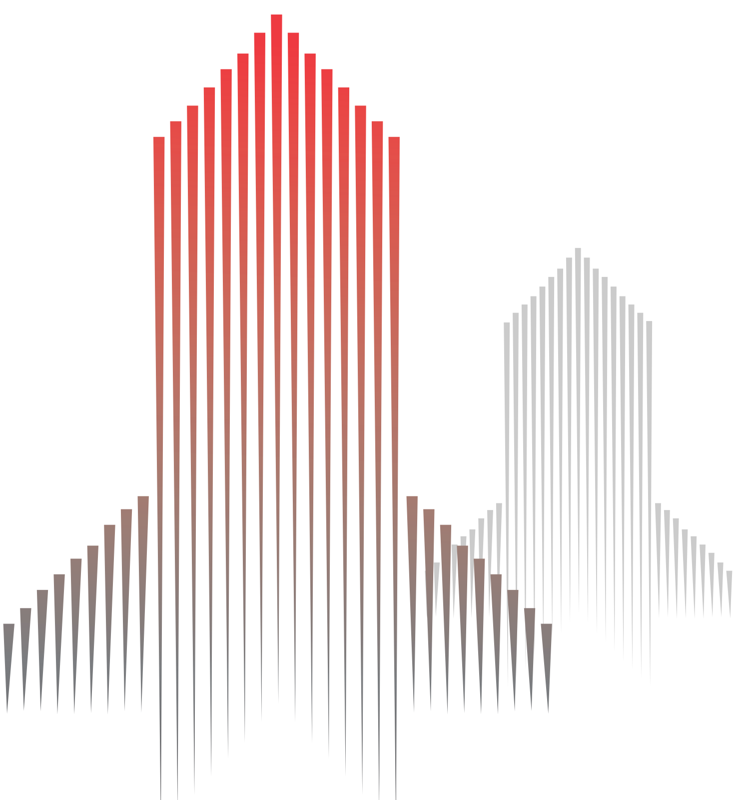
**ReaShure®**
Precision Release Choline

TAKE THE **REAL RESULTS CHALLENGE** TODAY

# Launch Her Lactation with ReaShure

Transition is the most important 6 weeks in your cow's lactation. The three weeks before calving and three weeks after calving set the trajectory for the entire lactation. With very few ways to positively impact the lactation curve after she reaches peak, sound investments made during this short 42-day transition period will reap rewards throughout the entire lactation.

ReaShure® *Precision Release Choline* is proven to deliver the choline essential for a fast start and a more efficient and productive lactation. New research from the University of Florida shows an average of 4.6 lbs more milk per day during the 40-week trial period. That's an additional 1,288 lbs per cow in just the first 40 weeks of lactation.



## Take the **Real Results Challenge** Today

### See the Results for Yourself

Try ReaShure in your transition cow ration for 90 days and we're confident you'll see results.

1. Sign up for the **Real Results Challenge** with your Balchem representative.
2. Feed ReaShure® *Precision Release Choline* to your transition group for 90 days at 60 gms/hd/day.
3. Monitor key health and performance parameters and report them using the **Real Results Challenge** rebate form (supplied by your Balchem Representative).
4. Receive your ReaShure Rebate of $0.75/lb fed.
5. Profit from the benefits of ReaShure throughout the entire lactation.

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# ReaShure®
Precision Release Choline

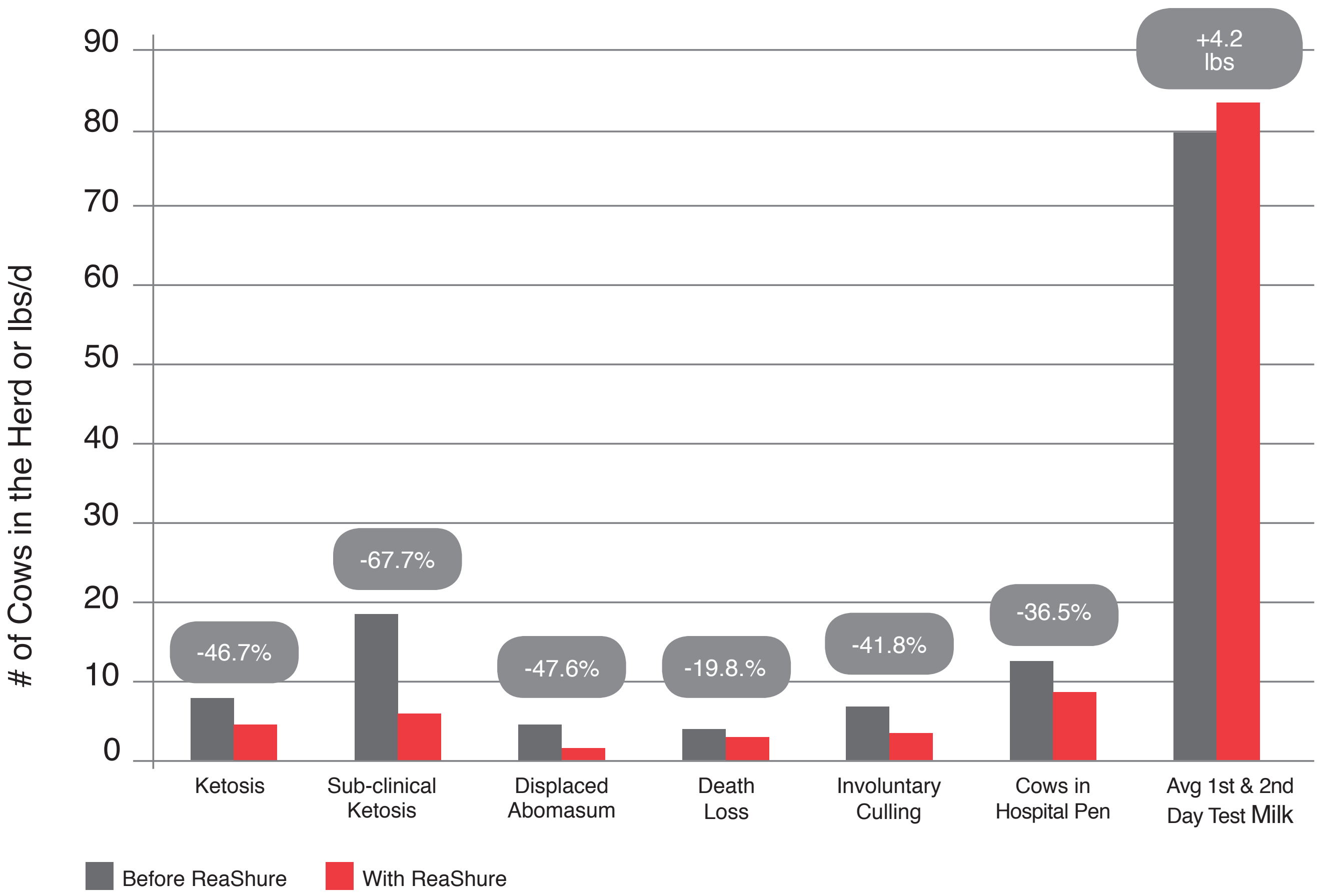
OVER 160,000 COWS TOOK THE CHALLENGE

**Documented results from past Real Results Challenge farms show dramatic impact.**

Over 160,000 cows have participated in the ReaShure **Real Results Challenge** on-farm trial. These herds have reported an average increase in milk production of 4.2 pounds/head/day. Producers also reported health benefits including reduced incidence of ketosis, displaced abomasum, involuntary culls and death loss.

**Get started today. Contact your Balchem representative or send a request to anh.marketing@balchem.com**

*Figure 1* **On-Farm Results with ReaShure**





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ReaShure®
Precision Release Choline



# Launch Milk Production to New Heights for Sustained Profitability

Glen Aines, Ph.D., *Global Ruminant Health Business Manager* | Kim Keesey, *Dairy Field Marketing*

A successful lactation is similar to the successful flight of a rocket. It must start fast and accelerate quickly to reach the highest possible peak, and then follow a sustained glide path to a successful landing. If anything goes wrong during launch, the results can be catastrophic at worst but at the very least result in the rocket not achieving the desired peak.

In dairy cattle, the launch of a cow's lactation begins with the transition period. A smooth, trouble-free transition can boost peak milk production, increasing the altitude from which the trajectory and glide path of her lactation begins. From that higher peak and elevated lactation curve, she'll see increased milk production for the entire lactation. If cows fail to transition smoothly and accelerate quickly to a high peak, there is very little you can do after the peak is reached to change the trajectory of the lactation curve or increase total lactation milk output. Sound investments made during this short 42-day transition period will reap rewards throughout the entire lactation.

## Choline's Role in a Successful Transition

Choline is a required nutrient that enables cows to utilize the fat (NEFA) mobilized from body stores. Production of NEFA is the cows' natural way of managing negative energy balance during the early stages of lactation and is a primary source of energy for many functions. Issues occur when the cow's liver cannot effectively process all the NEFA being mobilized, which can adversely affect its function. This leads to increased ketones in the blood (ketosis) which can negatively impact feed intake and further exacerbate negative energy balance, leading to even more NEFA mobilization.

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## Previous Research Measured the Benefits of Feeding Choline During the Transition Period

Results from 13 previous controlled and peer-reviewed studies reported improvements in milk production and component yields (Table 1). These studies only followed milk production through early lactation, leaving experts to only speculate about potential benefits over an entire lactation.

*Table 1*

**Summary of 13 trials on Rumen Protected Choline**

| Measurement | Control | Rumen Protected Choline | Difference | SEd | P = |
|---|---|---|---|---|---|
| DMI, lb/d | 39.98 | 41.60 | +1.62 | .46 | .0042 |
| Milk, lb/d | 70.88 | 75.75 | +4.87 | .75 | <.0001 |
| ECM, lb/d | 76.87 | 82.78 | +5.91 | 1.33 | .0038 |
| Fat yield, lb/d | 2.788 | 3.042 | +0.254 | .086 | .021 |
| Protein yield, lb/d | 2.300 | 2.467 | +0.167 | .053 | .010 |

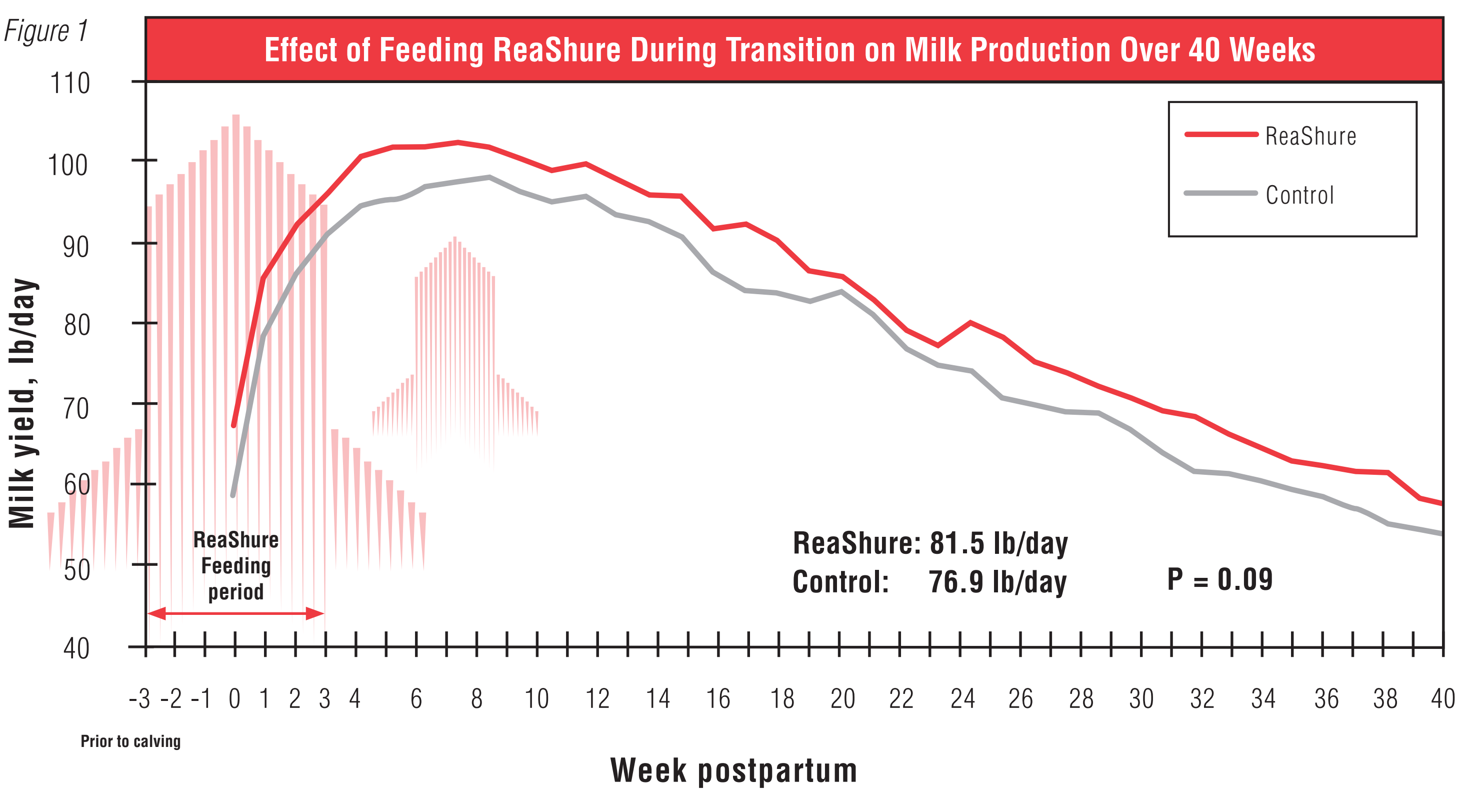
*Analytics completed by Ric R. Grummer, Ph.D. Emeritus Professor, Department of Dairy Science, University of Wisconsin-Madison*

## New Research Shows ReaShure's Benefits Extend Throughout the Entire Lactation

New research from the University of Florida (Zenobi et. al., 2017) has discovered that the benefits of feeding ReaShure® *Precision Release Choline* during the transition period extend throughout the entire lactation, and possibly even beyond. Cows fed ReaShure during the transition period had higher peaks and produced an additional 4.6 pounds of milk per day during the 40-week trial period, resulting in 1,288 pounds of milk per cow.

Other benefits noted in this study for cows fed ReaShure included; higher first service conception rates, significantly higher IgG levels in the colostrum, significantly faster rates of gain (0.09 lb/day) of heifers exposed to ReaShure in utero, and surprisingly a lower incidence rate of subclinical hypocalcemia (low blood calcium levels post-calving).

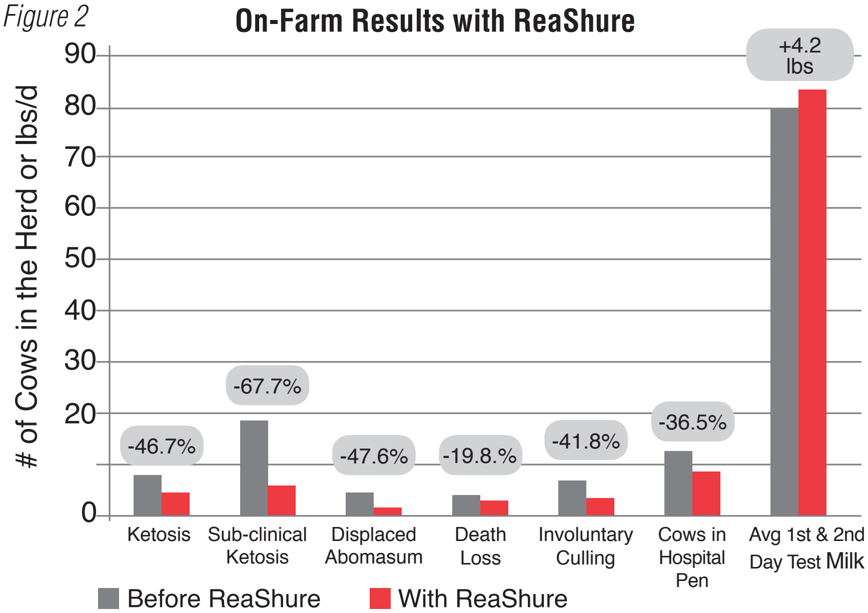
*Figure 1*



## Real Results on Real Dairies

Documented results from commercial dairies are virtually identical to those seen from university studies. Over 160,000 cows have participated in the ReaShure Real Results Challenge (90 day on-farm demonstration trials). These herds have reported an average increase in milk production of 4.2 pounds/head/day. Additionally, producers reported health benefits including reduced incidence of ketosis, displaced abomasum, involuntary culls and death loss (Figure 2).

*Figure 2*




### Health Benefits

As observed in the Real Results Challenge and reported in research literature, the benefits of feeding ReaShure extend far beyond just increased milk production. Improving the liver's ability to process the NEFA surge experienced during transition helps cows avoid metabolic disease, providing for a smoother start to their lactation.

## What is My Return on Investment (ROI) When Feeding ReaShure?

ReaShure is fed only during the 42-day transition period (21 days pre-fresh to 21 days post-fresh) to help cows transition more smoothly into lactation. Recent research shows, and field studies confirm, the benefits of a smoother transition are maintained throughout the entire lactation. The chart below (Table 2) demonstrates a potential return on your investment based on the results seen in the University of Florida study (Zenobi et al., 2017 in press).

*Table 2*

only $0.05/day[1]

**EXAMPLE**

| INVESTMENT | lbs Fed | | Cost/lb | | Total Cost |
|---|---|---|---|---|---|
| Additional Feed *(305 days[2])* | 470 lbs[3] | x | $0.10 | = | $47.00 |
| ReaShure *(42 days)* | 5.55 | x | $2.50 | = | $13.87 |
| | | | Investment | | $60.87 |

| REVENUE | Additional Milk | | Milk Price | | Total |
|---|---|---|---|---|---|
| 4.6 lbs milk x 305 days[4] = | 1,403 lbs | x | $ 0.17 | = | $238.51 |
| | **Revenue** | | **Investment** | | **Return/Cow** |
| | $238.51 | - | $ 60.87 | = | $177.64 |
| | **No. Cows** | | **Return/Cow** | | **Total Return** |
| | 500 | x | $177.64 | = | **$88,820** |

[1]when factored over 305 days of response
[2]15 week results extrapolated over 305-day lactation
[3]1.54 lbs x 305 days
[4]40 week results extrapolated over 305-day lactation

**CALCULATE YOUR RETURN**

| INVESTMENT | lbs Fed | | Cost/lb | | Total Cost |
|---|---|---|---|---|---|
| Additional Feed | 470 lbs[3] | x | $ | = | $ |
| ReaShure in Transition | 5.55 | x | $ | = | $ |
| | | | Investment | | $ |

| REVENUE | Additional Milk | | Milk Price | | Total |
|---|---|---|---|---|---|
| 4.6 lbs milk x 305 days[4] = | 1,403 lbs | x | $ | = | $ |
| | **Revenue** | | **Investment** | | **Return/Cow** |
| | $ | - | $ | = | $ |
| | **No. Cows** | | **Return/Cow** | | **Total Return** |
| | | x | $ | = | $ |

Healthy cows eat more feed!

## How Does ReaShure Compare to Other Widely Used Products?

With the tremendous number of feed additives on the market today, it's important to compare costs and potential returns (Table 3). Your investment in ReaShure is limited to the short 42-day transition period but benefits extend throughout the entire lactation, significantly impacting milk production and ROI.

*Table 3*

| | Cost $/d | Milk Yield lb/h/d | Increased Milk Income $/h/d[2] | ROI |
|---|---|---|---|---|
| ReaShure | $0.05[1] | 4.60 | $0.78 | 17.3 - 1 |
| Monensin | $0.03 | 1.54 | $0.26 | 8.1 - 1 |
| rBST | $0.45 | 10.00 | $1.70 | 3.8 - 1 |
| Rumen Bypass Fat | $0.60[3] | 4.50 | $0.77 | 1.3 - 1 |

[1]Cost calculated per day for a 305-day lactation.
[2]Milk Price $0.17/lb
[3]1 lb feeding rate.

## Summary

The success or failure of an entire lactation is often determined during the 42-day transition period. The health and well-being of the cow during the transition period will determine the amount of peak milk production, which in turn will predetermine the height and trajectory of the remaining lactation curve. Furthermore, very little can be done to positively alter that trajectory once the peak has been attained.

The key to maximizing milk production starts with investing your time, effort and resources during the transition period. Focus on those management practices that impact cow comfort, health and productivity. Include ReaShure® *Precision Release Choline* during the short 42-day transition window to help fuel a successful launch, high peak and elevated flight path for her lactation.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# Launch Your Cow's Lactation to New Heights

A successful lactation is very similar to the successful flight of a rocket. It must start fast and accelerate quickly to reach the highest possible peak, and then follow a sustained glide path to a successful landing. In dairy cattle, the launch of a cow's lactation begins with the transition period. A smooth, trouble-free transition can boost peak milk production, increasing the altitude from which the trajectory and glide path of her lactation begins. From that higher peak and elevated lactation curve, she'll achieve increased milk production for the entire lactation.

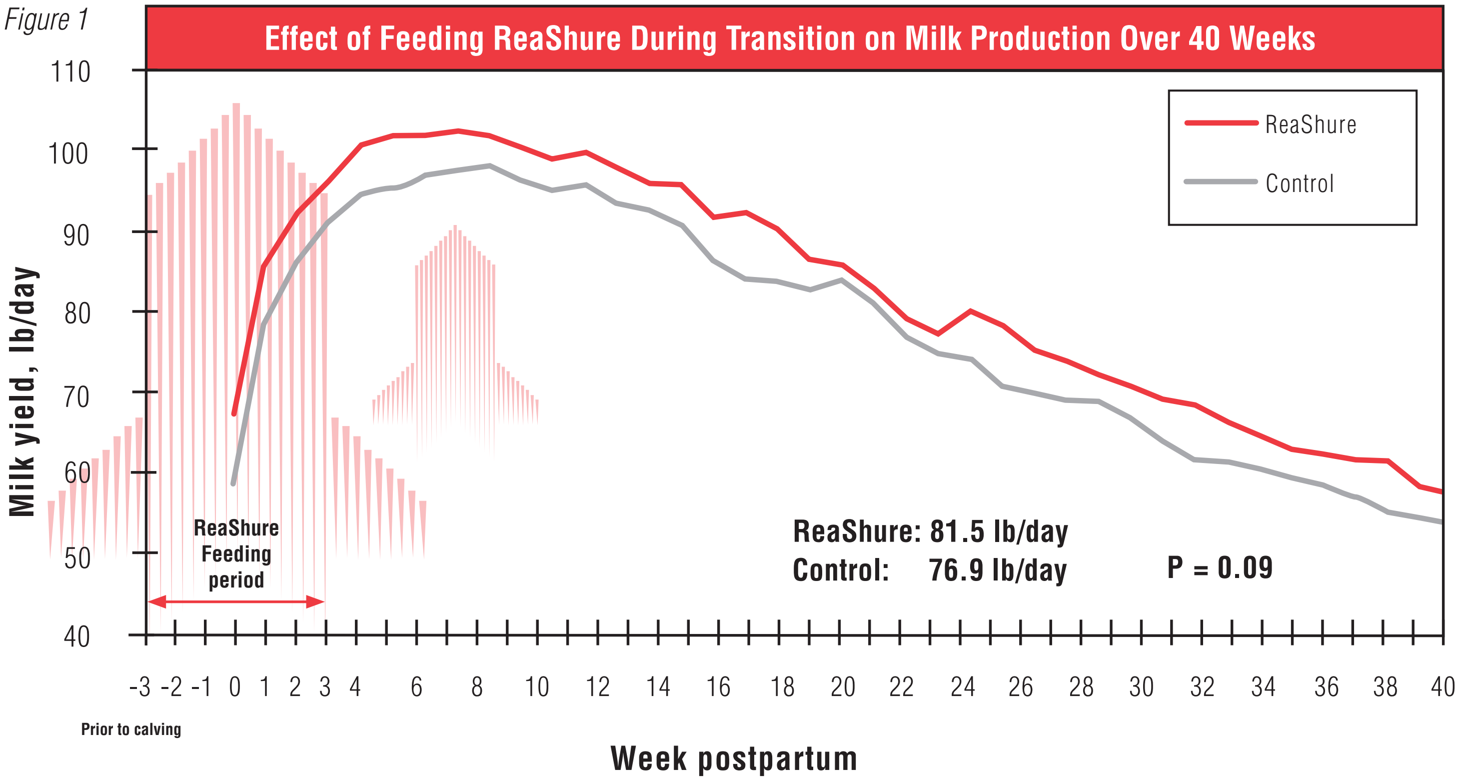
## Research Shows Benefits Extend Throughout Entire Lactation

New research from the University of Florida (Figure 1) demonstrates cows fed ReaShure during the transition period had higher peaks and produced an additional 4.6 pounds of milk per day during the 40-week trial period. If we extrapolate these results over a 305-day lactation, the outcome would be an additional 1,403 lbs of milk per cow per year.

### Results

- Higher peak milk production
- 4.6 lbs/cow/day more milk
- 1,403 lbs/cow for entire lactation

*Figure 1*



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# FULL LACTATION ECONOMICS

## Return on Investment (ROI)

ReaShure is fed only during the 42-day transition period (21 days pre-fresh to 21 days post-fresh) to help cows transition more smoothly into lactation. The chart below demonstrates a potential return on your investment based on the results seen in the University of Florida study (Zenobi et al., 2017 in press).

*Table 1*

**EXAMPLE**

only $0.05/day[1]

| INVESTMENT | lbs Fed | | Cost/lb | | Total Cost |
|---|---|---|---|---|---|
| Additional Feed *(305 days[2])* | 470 lbs[3] | x | $0.10 | = | $47.00 |
| ReaShure *(42 days)* | 5.55 | x | $2.50 | = | $13.87 |
| | | | Investment | | $60.87 |

| REVENUE | Additional Milk | | Milk Price | | Total |
|---|---|---|---|---|---|
| 4.6 lbs milk x 305 days[4] = | 1,403 lbs | x | $ 0.17 | = | $238.51 |
| | Revenue | | Investment | | Return/Cow |
| | $238.51 | - | $ 60.87 | = | $177.64 |
| | No. Cows | | Return/Cow | | Total Return |
| | 500 | x | $177.64 | = | **$88,820** |

[1]when factored over 305 days of response
[2]15 week results extrapolated over 305-day lactation
[3]1.54 lbs x 305 days
[4]40 week results extrapolated over 305-day lactation

## How Does ReaShure Compare to Other Widely Used Products?

Your ReaShure investment is limited to the short 42-day transition period but benefits extend throughout the entire lactation, significantly impacting total lactation milk production and ROI. The table to the right (Table 2) compares the relative return on investment from ReaShure as compared to other popular products.

*Table 2*

| | Cost $/d | Milk Yield lb/h/d | Increased Milk Income $/h/d[2] | ROI |
|---|---|---|---|---|
| ReaShure | $0.05[1] | 4.60 | $0.78 | 17.3 - 1 |
| Monensin | $0.03 | 1.54 | $0.26 | 8.1 - 1 |
| rBST | $0.45 | 10.00 | $1.70 | 3.8 - 1 |
| Rumen Bypass Fat | $0.60[3] | 4.50 | $0.77 | 1.3 - 1 |

[1]Cost calculated per day for a 305-day lactation.
[2]Milk Price $0.17/lb
[3]1 lb feeding rate.

## Summary

The success or failure of an entire lactation is often determined during the 42-day transition period. The health and well-being of the cow during the transition period will determine the amount of peak milk attained, which in turn will set the trajectory of the remaining lactation curve.

Include ReaShure® *Precision Release Choline* in your transition cow rations to help fuel a successful launch, high peak and elevated glide path for her lactation.

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TECHNICAL REPORTS

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## *Precision Release Choline* Feeding Recommendations



### Overview

Choline is an essential nutrient that functions in gene expression, nerve transmission, cell membranes, and lipid transport. The classic choline deficiency symptom is fatty liver. Choline deficiency during the transition period prevents adequate processing and export of fatty acids from the liver and to the mammary gland as very low density lipoproteins; hence fatty acids are diverted towards deposition as fat or conversion to ketone bodies such as beta-hydroxybutyrate, acetone, and acetoacetate.

Feeding ReaShure® *Precision Release Choline* during the transition period has been shown to be effective in improving liver function, reducing fatty liver, ketosis and energy related disorders (Strang et al., 1998; Lima et al., 2012). In contrast to nonruminants, dairy cows cannot be fed free dietary choline. Choline must be fed in a form that prevents extensive degradation by rumen micro-organisms. Feeding rumen-protected choline to transition dairy cows not only improves health; a summary of 13 transition cows studies indicates it also increases milk production by approximately 5 lb/day (Grummer, 2012).

### Recommended Feeding Rate

From early data obtained by Cornell University (Piepenbrink et al., 2003), it was concluded that 60 g/day of ReaShure was the best dose to benefit liver health and milk production. Since that study, the vast majority of transition cow trials have fed approximately 60 g /day both pre- and postpartum. Because there is a large data base with feeding the 60 g/day dose, there is confidence in recommending it and it is strongly recommended not to deviate from it. Jersey cattle are lighter, and it is often asked if a lower dose would be adequate. Perhaps, but a dose response study has not been conducted with Jersey cows. Therefore, 60 g/day is suggested for Jerseys and all other dairy breeds.

### Recommended Feeding Period

Dairy cows can synthesize choline endogenously; however, the transition period represents a window of time in which endogenous choline production is insufficient. This is due to the dramatic increase in NEFA uptake by the liver that begins at calving and continues post calving (*Figure 1*, Reynolds et al., 2003). *Figure 2* shows the progression of fat deposition in the liver of transition dairy cows and provides key insight into when choline is deficient. The greatest rate of fat deposition occurs during a surge in fatty acid mobilization on the day of calving. Choline deficiency may continue after calving as NEFA uptake by the liver remains elevated due to negative energy balance.

21 days *Prepartum* - feeding ReaShure for 21 days prepartum is recommended so that choline is circulating to the liver at the time of calving to help package and transport fat to the mammary gland while reducing deposition in the liver during the time when fat infiltration is greatest (*Figure 2;* Vazquez-Anon et al., 1994). If we knew the exact day of calving, feeding ReaShure 3-4 days prior to calving would probably be sufficient. Since we do not know the exact day of parturition, it is recommended to initiate feeding at 21 days prepartum to accommodate traditional prepartum grouping strategies.

21 days *Postpartum* - it is recommended that feeding ReaShure be continued for 21 days postpartum. Feeding postpartum will assist the liver exporting needed triglycerides to target tissues like the mammary gland, deplete fat that accumulated during parturition and help prevent further fat accumulation in the liver during negative energy balance *(Figure 2)*. Feeding ReaShure postpartum should continue until the period of greatest negative energy balance has

subsided and NEFA uptake by the liver is moderated to the extent that the endogenous supply of choline can adequately facilitate normal liver function. The length of this period will vary among herds and among cows within a herd. By 21 days postpartum, cows in most well managed herds will no longer experience dramatic elevations in NEFA uptake by the liver (e.g., see *Figure 1*); therefore, the need for feeding ReaShure is diminished.

Not all farms will have transition cow grouping strategies that precisely align with the ReaShure "recommended" feeding window of 21 days prepartum through 21 days postpartum. That should not preclude feeding ReaShure. For example, ReaShure should still be fed to prefresh groups that begin any time before 10 days prior to calving. Likewise, ReaShure should be fed to any postfresh group with the understanding that benefits may begin to be diminished after cows are beyond 21 days postpartum.

Also, some farms may not have a pre- and postpartum group. This should not preclude feeding ReaShure only during the prepartum period or only during the postpartum period! *Figure 3* shows expected results of feeding ReaShure prepartum only, postpartum only, and both pre- and postpartum on liver fat accumulation which is indicative of a choline deficiency and impaired liver function. Clearly, feeding pre- and postpartum would be most beneficial, but feeding either pre- or postpartum should provide benefits to the cow by improving liver function.

Topdressing ReaShure can be an option for some dairy farmers. ReaShure is palatable and readily consumed by the vast majority of cows when topdressed. Using computerized feeders to tailor feed ReaShure to designated cows is also a successful feeding strategy.

*Figure 1 Nonesterified fatty acid uptake (grams/day) by the liver during the transition period. Reynolds et al. 2003.*

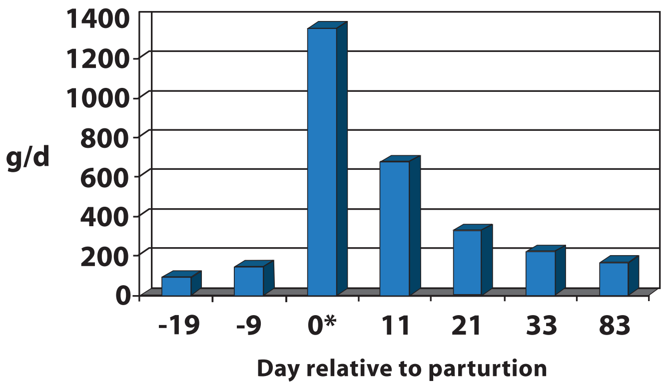



*Figure 2 Accumulation of fat in the liver during the transition period. Vazquez-Anon et al., 1994.*

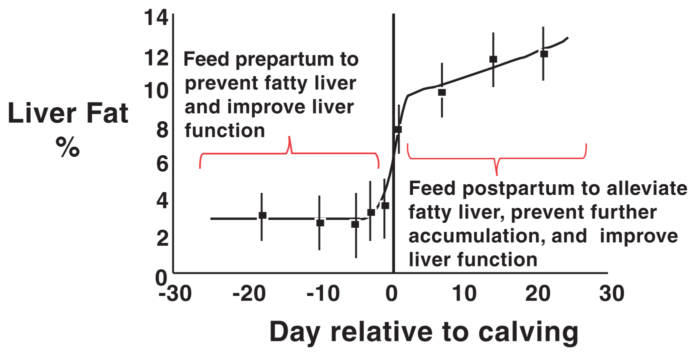
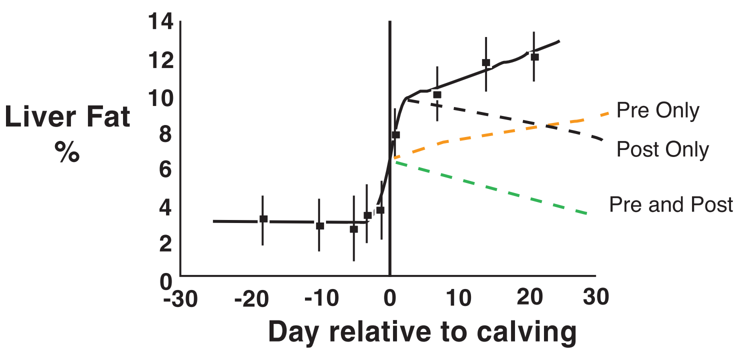



*Figure 3 Projected results of feeding ReaShure pre-, post-, or pre- and postfresh on liver function and liver fat content in transition cows.*

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# RESEARCH SUMMARIES

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Balchem Research Summary

# Effect of ReaShure rumen-protected choline on performance, blood metabolites, and hepatic triacylglycerols of periparturient dairy cattle[1]

A summary of research conducted by R. L. G. Zom, J. van Baal, R. M. A. Goselink, J. A. Bakker, M. J. de Veth, and A. M. van Vuuren. Wageningen UR Livestock Research, Netherlands published in the August 2011 issue of the Journal of Dairy Science (Volume 94, pages 4016 – 4027).

## Introduction

Fatty liver occurs in approximately 50-60% of dairy cows at or shortly after calving[2],[3]. It occurs because the cow mobilizes energy from adipose tissue in response to hormonal changes at calving and negative energy balance immediately after calving when the cow cannot consume enough energy to support maintenance and milk production. However, it can also occur anytime the cow experiences negative energy balance from other factors such as sickness, suboptimal environment (overcrowding, heat stress, poor stall design) or poorly formulated diets. When cows mobilize fat from adipose tissue, the resulting nonesterified fatty acids (NEFA) enter into blood and may be taken up by the liver. Ideally, most of these fatty acids would be exported from the liver as a constituent of very low density lipoproteins (VLDL) so that they could be transported to the mammary gland where they can support lactation. Choline is required for VLDL synthesis and export, but unfortunately, very little dietary choline escapes degradation by microorganisms in the rumen. Therefore, ruminants are naturally prone to development of fatty liver when the liver is exposed to high levels of NEFA. Livers containing elevated fat levels have lower rates of ammonia detoxification (ureagenesis) and glucose synthesis and cows with fatty liver have lower milk production, greater susceptibility to infectious diseases, higher incidences of ketosis, and poor reproductive performance[4]. The only practical way to avoid fatty liver and its consequences is to supplement diets with choline that has been protected from ruminal degradation.

Balchem Corporation manufactures a high quality, ruminally protected choline product called ReaShure(R) *Rumen Protected Choline.* The choline is encapsulated by fat which allows it to bypass the rumen and enter the small intestine. The environment in the small intestine allows for the majority of choline to be released from encapsulation for absorption into the blood stream. The classic deficiency symptom for choline in nonruminant animals is fatty liver. Since dairy cows normally have very low amounts of choline absorbed from the small intestine, experience large quantities of NEFA being delivered to the liver at and shortly after calving, and suffer from high rates of fatty liver, it is highly likely they are choline-deficient and could benefit from supplementation of ReaShure during the transition period.

## Methodology

The effects of feeding ReaShure rumen-protected choline on liver fat (specifically triglyceride), blood metabolites, feed intake and milk production were published in the August 2011 issue of the Journal of Dairy Science (Volume 94, pages 4016-4027). Thirty-eight multiparous Holstein Friesian dairy cows in good body condition (mean = 3.25) and not experiencing subclinical ketosis from the herd at Wageningen University and Research Center, Netherlands, were fed 60 g ReaShure/day or a control diet from 3 weeks prior to calving until 6 weeks postcalving. Cows were housed in groups and transponder controlled feeders were used to dispense 582 g soybean meal and 18 g palm oil per day to control cows and 540 g soybean meal and 60 g ReaShure per day to treatment cows. In addition to these treatments, a dry cow feed mixture (grass silage/ corn silage/wheat straw/soybean meal/premix) was consumed ad libitum and cows were gradually increased up to 8.1 kg (2 lb) DM of additional concentrate per day prior to calving. After calving, treatments continued and cows consumed a lactating cow feed mixture (grass silage/corn silage/grass seed straw/ soybean meal/ premix) ad libitum and were gradually increased from 2 to 17 lb of additional concentrate per day. Dry matter intake and milk production were measured daily and milk was sampled from four consecutive milkings each week. Blood samples were obtained weekly with additional samples taken at 1 and 4 days postpartum. Liver biopsies were obtained at 3 wk prior to calving and at week 1, 4, and 6 postcalving from a subset of eight animals per treatment.

## Results and Discussion

Immediately after calving, cows fed ReaShure consumed significantly more dry matter, 1.6 kg/day (3.6 lb), from the feed mixture fed (concentrate feeding from feeders was fixed). The advantage in dry matter intake remained for the entire trial; however, the difference for the 6 week postpartum period, 0.8 kg/day (1.8 lb), was not statistically significant *(Figure 1).* Feeding ReaShure increased milk protein yield immediately postpartum by 136 g/day. Body weight and body condition score of cows was not affected by treatment. Liver triglyceride concentration was significantly reduced by feeding ReaShure, primarily due to differences at 1 and 4 weeks after calving *(Figure 2)*.

The significant increase in milk protein yield was a reflection of greater milk yield, +2.0kg/day (4.4lbs)and milk protein percentage (+0.13 percentage units) when feeding ReaShure, although the differences in milk yield and milk protein percentage were not statistically significant. The greater milk protein yield may have been due to greater feed (i.e., nutrient) intake. Alternatively, it may have been a direct effect of feeding ruminally protected choline. Choline serves as a source of methyl groups for the resynthesis of methionine from homocysteine. Therefore, supplying more choline may spare methionine which is considered one of the most limiting amino acids for protein synthesis by early lactation dairy cows. The researchers who conducted this trial formulated the diets to be adequate in methionine, however, it is difficult to meet amino acid requirements immediately after calving when feed intake is low. Not surprisingly, the greatest advantage in milk protein yield from feeding ReaShure was during the first 20 days postpartum *(Figure 3)*.

The reduction in liver triglyceride from feeding ReaShure is consistent with previous research[5], and solidifies the role of choline in facilitating VLDL triglyceride export from the liver and reducing the likelihood of fatty liver in postpartum dairy cows. The absence of treatment effects on blood metabolites (e.g., NEFA) reinforces that choline has a direct favorable effect on liver metabolism.

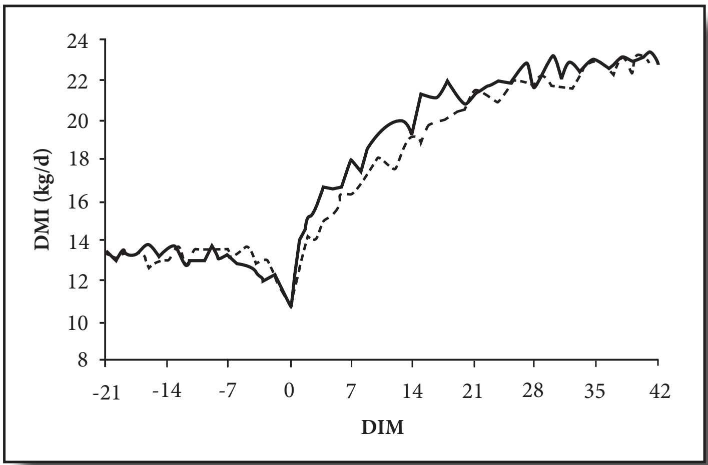
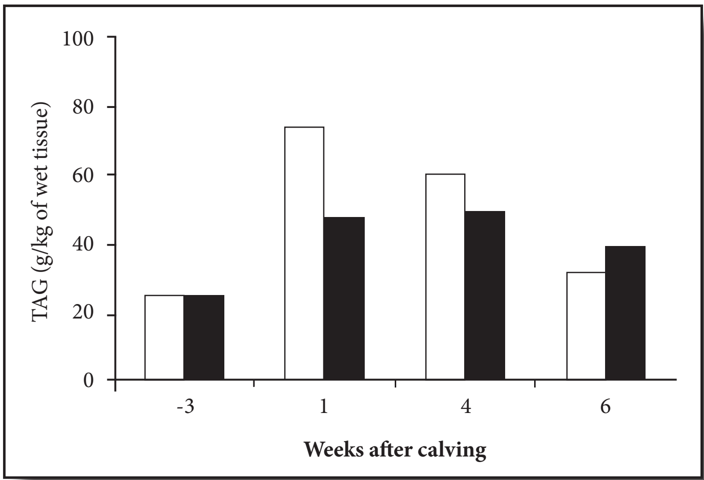



*Figure 1. Dry matter intake (DMI) of cows fed diets with (solid line) or without (dashed line) ReaShure rumen-protected choline at various days in milk (DIM).*

*Figure 2. Liver triglyceride (TAG) in cows fed diets with (black bars) or without (white bars) ReaShure rumen-protected choline.*



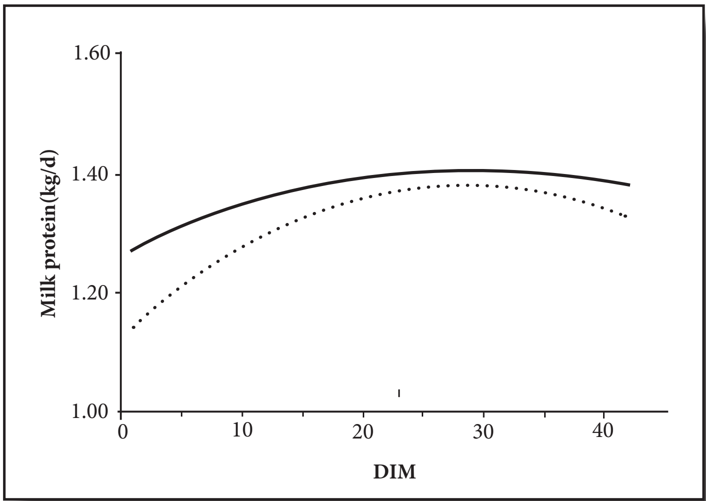




*Figure 3. Milk protein yield of cows fed diets with (solid line) or without (dashed line) ReaShure rumen-protected choline at various days in milk (DIM).*

## Conclusion

The results of this Dutch study and previous studies conducted in other countries[5,6,7] indicates that feeding ReaShure rumen-protected choline reduces fat accumulation in the liver and improves production under a wide variety of feeding and management systems. To view the entire research go to: http://www.journalofdairyscience.org/article/S0022-0302(11)00405-X/abstract.

## References

[1] Zom, R. L. G, J. van Baal, R. M. A. Goselink, J. A. Bakker, M. J. de Veth, and A. M. van Vuuren. 2011. Eff ect of rumen-protected choline on performance, blood metabolites, and hepatic triacylglycerols of periparturient dairy cattle. J. Dairy Sci. 94:4016-4027.

[2] Grummer, R. R. 1993. Etiology of lipid related metabolic disorders in periparturient dairy cattle. J. Dairy Sci. 76:3882-3896.

[3] Jorritsma, R., H. Jorritsma, Y. H. Schukken, P. C. Bartlett, T. Wensing, and G. H. Wentink. 2000. Prevalence and indicators of post partum fatty infi ltration of the liver in nine commercial dairy herds in The Netherlands. Livest. Prod. Sci. 68:53-60.

[4] Grummer, R. R. 2006. Etiology, pathophysiology, and prevention of fatty liver in dairy cows. Pages 141-153 in Production Diseases in Farm Animals. N. P. Joshi and T. H. Herdt, eds. Wageningen Academic Publishers, Wageningen, The Netherlands.

[5] Cooke, R. F., N. S. Del Rio, D. Z. Caraviello, S. J. Bertics, M. H. Ramos, and R. R. Grummer. 2007. Supplemental choline for prevention and alleviation of fatty liver in dairy cattle. J. Dairy Sci. 90:2413-2418.

[6] Lima, F. S., M. F. Sa Filho, L. F. Greco, F. Susca, V. J. A. Magalhaes, J. Garrett, and J. E. P. Santos. 2007. Eff ects of feeding rumen-protected choline (RPC) on lactation and metabolism. J. Dairy Sci. 90 (Suppl. 1):174.

[7] Zahra, L. C., T. F. Duffi led, K. E. Leslie, T. R. Overton, D. Putnam, and S. J. LeBlanc. 2006. Eff ects of rumen-protected choline and monensin on milk production and metabolism of periparturient cows. J. Dairy Sci. 89:4808-4818.

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Balchem Research Summary

# Meta-analysis of Transition Cow Studies Examining the Effects of Supplementing Rumen-protected Choline to Transition Dairy Cows.

Ric R. Grummer, Ph.D. Ruminant Technical Director, Balchem Corp.

## Introduction

Meta-analysis is a statistical approach to combine the results of several studies that had a common research objective. Pooling data across studies allows for wider inference for conclusions and may increase the statistical power for determining treatment effects. In theory, individual research studies should have sufficient replication and statistical power to adequately test a hypothesis. However, in reality, replication often is not adequate yet the research survives peer-review and is published. Transition cow studies are notorious for insufficient replication. This often occurs because university research herds are not of adequate size to provide sufficient animal numbers during the period of time allotted for the study. Often times, multiple studies are summarized by simply reporting a mean response across studies. This is too simplistic and can lead to erroneous conclusions. An appropriate meta-analysis should account for variation among studies, include variables that may explain variation, and weight studies according to size and amount of variation among experimental units (studies with more replication and less variation are more influential than studies with less replication and more variation).

A meta-analysis of studies examining the effects of rumen-protected choline (RPC) on milk production recently was published in the Journal of Dairy Science (93:3746; Sales et al., 2010). There were some problems with the methodology used in this paper and the authors included studies that utilized cows that were beyond the transition period. Since that analysis, more studies have been conducted and we now have a reasonably large number of studies in which RPC was fed to transition cows. The objective of the current meta-analysis was to restrict the study selection to those in which RPC was fed during times that are most consistent with our feeding recommendations, i.e., the transition period.

## Methodology

For meta-analysis, criteria for study selection are extremely important and must be clearly defined. For studies to be included in this analysis, RPC had to be fed *prior* to calving. Studies were *not* restricted to those supplementing ReaShure, however the majority of studies did use ReaShure. Feed stability or evidence of bioavailability of choline source was not a criterion for study selection. For example, the study of Hartwell et al. (2001; utilizing Capshure. Balchem Corp) was included even though the RPC source is known to be inferior to ReaShure. Studies were not screened for "soundness" of research. To qualify, studies had to report treatment means and a measure of variation that accounted for sample size (standard error of the mean).

For some studies, this eliminated response variables that were presented in graphic form. Ten of the thirteen trials were published in peer-reviewed journals. One trial from Oelrichs et al. and two studies of Lima et al. *(Table 1)* were used because we have copies of unpublished manuscripts corresponding to those trials.

*Table 1. Studies used in the Meta-Analysis. Studies shaded have not been published in a peer-reviewed journal.*

| Study | Choline Dose, g/d | Product | Duration | Exp. Units | Parity |
|---|---|---|---|---|---|
| Hartwell | 0,6,12 | Capshure | -21 to 120 | 24 | M |
| Zom et al. | 0,15 | ReaShure | -21 to 42 | 19 | M |
| Lima et al. #1 | 0,15 | ReaShure | -25 to 80 | 4 (pen) | M,P. |
| Lima et al. #2 | 0,15 | ReaShure | -22 to 0 | 5 (pen) | P |
| Oelrichs et al. | 0,15 | ReaShure | -28 to 100 | 32 | M,P. |
| Zahra et al. | 0,14 | ReaShure | -25 to 28 | 91 | M,P. |
| Piepenbrink et al. | 0,11,15,19 | ReaShure | -21 to 63 | 12 | M |
| Janovick et al. | 0,15 | ReaShure | -21 to -21 | 21 | M |
| Eleket al. | 0, 25/50 pre/post | Norcol-25 | -25 to 60 | 16 | M,P. |
| Ardalan et al. | 0,14 | Col 24 | -28-70 | 20 | M,P. |
| Pinotte et al. | 0,20 | Overcholine 45% | -14 to 30 | 13 | M |
| Xu et al. #1 | 0,7.5 | Not reported | -7 to21 | 7 | M |
| Xu et al. #2 | 0,11,22,33 | Not reported | -15 to 15 | 9 | M,P. |

Time when RPC supplementation was started varied between 28 to 7 days prior to expected calving. RPC supplementation was terminated anywhere from the day of calving to 120 days in milk.

Response variables included DMI, milk yield, energy corrected milk yield, fat %, protein %, and fat and protein yield. Insufficient data was available for analysis of liver fat or energy-related blood parameters.

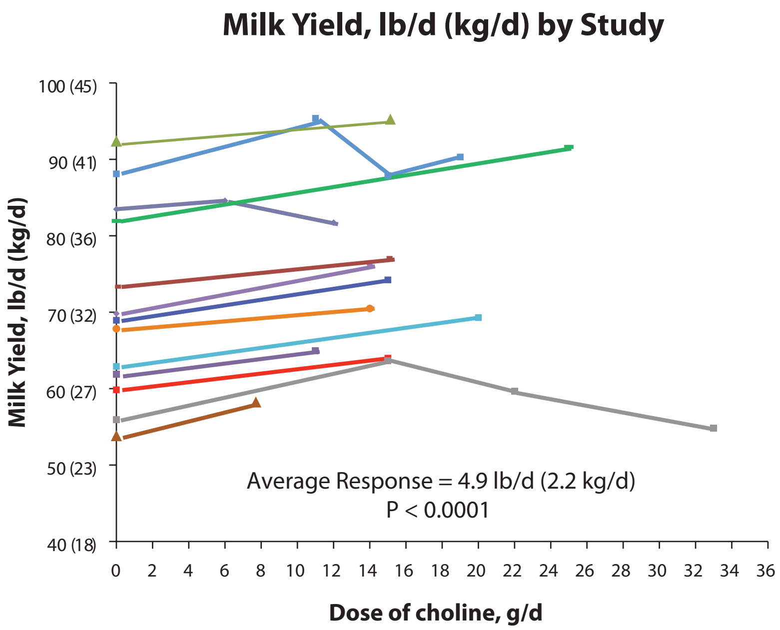
## Results and Discussion

Feeding RPC to transition cows increased dry matter intake and milk, energy-corrected milk, protein and fat yield *(Table 2)*. Milk components (expressed as a percentage) were not affected by feeding RPC to transition dairy cows. Reasons for the increases in dry matter intake and milk yield are not known, but they may reflect cows with a healthier liver. For example, a liver with lower fat content may synthesize more glucose which is a precursor for lactose, the milk component that dictates milk yield. The consistency in responses across studies *(Figure 1)* supports the concept that choline is a limiting nutrient in transition cow diets. One would be hard pressed to find a more consistent response to a nutrient in the scientific literature.

*Table 2. The effects of feeding RPC to transition cows on dry matter intake and milk.*

| | Control | RPC | SEd | P = |
|---|---|---|---|---|
| DMI, lb/d (kg/d) | 39.98 (18.15) | 41.60 (18.15) | .46 (.21) | .0042 |
| Milk, lb/d (kg/d) | 70.88 (32.18) | 75.75 (34.39) | .75 (.34) | <.0001 |
| ECM, lb/d (kg/d) | 76.87 (34.9) | 82.78 (37.58) | 1.33 (.72) | .0038 |
| Fat yield lb/d (kg/d) | 2.788 (1.266) | 3.042 (1.381) | .086 (.039) | .021 |
| Protein yield, lb/d (kg/d) | 2.300 (1.044) | 2.467 (1.120) | .053 (.024) | .010 |

*Figure 1. Milk responses to feeding RPC*




(Since the studies of Oelrichs et al. and Lima et al. are not published, an additional analysis was conducted without them. This did not change the interpretation of the analysis. Attempts were made to see if conclusions could be made about duration of treatment or parity; however, more studies (i.e. replication) will be needed to draw conclusions regarding these parameters.)

## References


Ardalan, M., M. Dehghan-banadaky, K. Rezayazdi, and N. Ghavi Hossein Zadeh. 2011. The effect of rumen-protected methionine and choline on plasma metabolites of Holstein dairy cows. J. Agric. Sci. doi:10.1017/S0021859610001292.

Elek, P., J. R. Newbold, T. Gaal, L. Wagner, and F. Husveth. 2008. Effects of rumen-protected choline supplementation on milk production and choline supply of periparturient dairy cows. Anim. 2:1595-1601.

Hartwell, J. R., M. J. Cecava, and S. S. Donkin. 2000. Impact of dietary rumen undegradable protein and rumen-protected choline on intake, peripartum liver triacylglyceride, plasma metabolites and milk production in transition dairy cows. J. Dairy Sci. 83:2907-2917.

Janovick Guretzky, N. A., D. B. Carlson, J. E. Garret, and J. K Drackley. 2006. Lipid metabolite profiles and milk production for Holstein and Jersey cows fed rumen-protected choline during the periparturient period.J. Dairy Sci. 89:188-200.

Lima, F. S., M. F. Sa Filho, L. F. Greco, F. Susca, V. M. Magalhaes, and J. E. P. Santos. Effects of feeding rumen-protected choline on metabolismand lactation of transition dairy cows. Manuscript prepared.

Oelrichs, W. A., M. C. Lucy, M. S. Kerley, and J. N. Spain. Production and reproduction of dairy cows fed rumen-protected choline during the periparturient period. Manuscript prepared. Piepenbrink, M. S., and T. R. Overton. 2003. Liver metabolism and production of cows fed increasing amounts of rumen-protected choline during the periparturient period. J. Dairy Sci. 86:1722-1733.

Pinotti, L., A. Baldi, I. Politis, R. Rebucci, L. Sangalli, and V. Dell'Orto. 2003. Rumen-protected choline administration to transition dairy cows: effects on milk production and vitamin E status. J. Vet. Med. A 50:18-21.

Sales, J., P. Homolka, and V. Koukolova. 2010. Effect of dietary choline on milk production of dairy cows: A meta-analysis. J. Dairy Sci. 93:3746-3754.

St-Pierre, N. R. 2001. Integrating quantitative findings from multiple studies using mixed model methodology. J. Dairy Sci. 84:741-755.

Xu, G., J. Ye, J. Liu, and Y. Yu. 2006. Effect of rumen-protected choline addition on milk performance and blood metabolic parameters in transition dairy cows. Asian-Aust. J. Anim. Sci. 19:390-395.

Zahra, L. C., T. F. Duffiled, K. E. Leslie, T. R. Overton, D. Putnam, and S. J. LeBlanc. 2006. Effects of rumen-protected choline and monensin on milk production and metabolism of periparturient cows. J. Dairy Sci. 89:4808-4818.

Zom, R. L. G., J. van Baal., R. M. A. Goselink, J. A. Bakker, M. J. de Veth, and A. M. van Vuuren. 2011. Effect of rumen-protected choline on performance, blood metabolites, and hepatic triacylglycerols of periparturient dairy cattle. J. Dairy Sci. 94:4016-4027.



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Balchem Research Summary

# Effect of feeding rumen protected choline on performance, health and reproduction of dairy cows.

A summary of a study conducted by F. S. Lima, M. F. Sá Filho, L. F. Greco and J.E. P. Santos. University California-Davis. Published as ADSA abstracts (2007, 2008), Florida Ruminant Nutrition Conference Proceedings (2009) and The Veterinary Journal (2011).

## Background

At calving, dairy cows go from a period of positive energy balance to negative energy balance. There is a surge in blood non-esterified fatty acids (NEFA) at calving, due to the stress and the hormonal changes associated with parturition and initiation of lactation. Blood NEFA remains elevated after calving due to the mobilization of adipose tissue (NEFA) to meet the cow's energy needs. A portion of blood NEFA is taken up by liver and oxidized for energy while some is re-assembled into a triglyceride (TG) and exported from the liver as a constituent of very low density lipoproteins (VLDL). The amount of NEFA that can be handled by these two pathways is limited in ruminants; consequently some of the NEFA is partially oxidized resulting in elevated ketones in the blood. Also, since the export of TG via the VLDL is limited, TG will accumulate in the liver, leading to impaired liver function. Providing the transition dairy cow with rumen protected choline has been shown to alleviate fatty liver, presumably by supplying additional choline is an essential component of VLDL. Enhancing TG export from the liver should also reduce the conversion of NEFA to ketones and consequently ketosis.

## Objective and Design

A trial was conducted to determine if feeding ReaShure® Precision Release Choline during the transition period could improve lipid metabolism, reduce the incidence of clinical and subclinical ketosis and other energy related disorders, and improve the fertility of the cows. The trial was conducted at a commercial dairy in California.

A control diet or one supplemented with ReaShure (60 gm/cow/day) was fed to 369 primi- and multiparous Holstein dairy cows from 25 days prepartum to 80 days postpartum. Cows were housed in pens. Cows were blocked by parity and expected day of calving, and within each block, randomly assigned to treatments. Parameters monitored included pen dry matter intake (DMI), milk production and composition, health, and reproductive status. Cows were evaluated daily to diagnose diseases. Diseases monitored included: retained placenta, metrtitis, displaced abomasum, mastitis, and ketosis (clinical and subclinical) as well as required treatments. Clinical ketosis was characterized by a lack of appetite, depressed attitude and presence of severe ketonuria. Subclinical ketosis was characterized by monitoring plasma beta-hydroxy butyric acid (BHBA) at day 1 and 14 post-calving. Subclinical ketosis was characterized as BHBA levels exceeding 1000, micro mol/L. Body Condition score (BCS) was monitored pre- and postpartum using a scale of 1 to 5. A liver biopsy was collected on a subset of cows in each treatment group between day 7 to 10 post-calving and analyzed for TG. All cows had their estrous cycle presynchronized and then 10 days later cows were enrolled in a timed insemination (AI) protocol. Pregnancies per AI were evaluated at 30 and 65 days after first insemination and at 38 days after the second insemination.

## Results

TDMI pre-calving did not differ between treatments and averaged 12.5 kg/d (Table 1). After calving, cows fed ReaShure had a higher DMI (P = 0.10) than control cows (23.9 vs. 22.6 kg/d). Feeding ReaShure improved 3.5% fat corrected milk (FCM) yield (44.6 vs. 42.8 kg/d) as depicted in Table 1. Milk fat and protein % were not different between treatments; but milk fat and protein yield were increased by ReaShure feeding. Yield of milk fat for ReaShure fed cows was 1.61 kg/day vs. Control of 1.52 kg/day (P = 0.05) and yield of true protein for ReaShure fed cows was 1.21 kg/day vs. 1.17 kg/day for control cows (P = 0.08). Cows lost approximately 0.75 units of BCS from enrollment to 90 d postpartum, and feeding ReaShure reduced (p= 0.01) BCS losses postpartum.

The incidences of clinical ketosis (P < 0.01) and the relapse of clinical ketosis (P < 0.05) were also reduced for ReaShure vs. control cows. Prevalence of SCK at day 1 postpartum (as indicated by plasma BHBA) tended to be less (P < 0.07) for ReaShure than control cows, regardless of parity. At day 14, prevalence of subclinical ketosis was reduced (P= 0.05) by feeding ReaShure in the multiparous cows, as indicated by a parity by treatment interaction. From the liver biopsy, if cows had greater than 5% fat in the liver tissue, they were classified as having hepatic lipidosis. Less (P < 0.05) of the cows fed ReaShure were classified as having hepatic lipidosis than those in the control group (Table 2).

Feeding ReaShure did not influence the incidence of retained placenta, fever, metrtitis, and displaced abomasum (DA). Feeding ReaShure tended to reduce the incidence of mastitis (P= 0.06) and significantly reduced (P= 0.02) the number of mastitis cases per cow (Table 2). When considering all of the postpartum health disorders (retained placenta, metritis, clinical ketosis, DA, and mastitis), cows consuming ReaShure experienced lower (P < 0.001) morbidity than control treatment cows (Table 2). An interaction (P= 0.05) was observed between treatment and parity for cyclic status. Pregnancy at first service was numerically higher for cows fed ReaShure than control but did not reach statistical significance (P = 0.20).

## Discussion

Fatty liver and ketosis (clinical and subclinical) are metabolic disorders common to transition cows and have been associated with depressed feed intake, lower milk production, poor immune response and reproductive performance, and impaired liver function including depressed glucose production. Therefore, monitoring fatty liver or ketosis can be used to assess transition cow well-being and performance.

In this trial, feeding of ReaShure during the transition period reduced the incidence of hepatic lipidosis. Cows in this treatment group ate 1.3 kg/d more DM than control cows and produced 1.8 kg/d more 3.5% FCM for the first 80 days-in-milk. The lower incidence of hepatic lipidosis in the ReaShure fed cows was also accompanied by a reduction in the incidence of clinical and subclinical ketosis, mastitis, and overall morbidity vs. control cows. Evidence of an improvement in reproductive status with ReaShure was not statistically significant (P = 0.20); but ReaShure fed cows had an improved pregnancy rate at first AI. These responses indicate that the cows fed ReaShure were healthier and more productive than control cows.

*Table 1. Milk production and composition, and dry matter intake.*

| | Control | | ReaShure® | | P Value |
|---|---|---|---|---|---|
| Milk, lb/d (kg/d) | 92.8 | (42.1) | 95.0 | (43.1) | 0.09 |
| 3.5% FCM, lb/d (kg/d) | 94.4 | (42.8) | 98.3 | (44.6) | 0.04 |
| ECM, lb/d (kg/d) | 84.9 | (38.5) | 88.4 | (40.1) | 0.04 |
| Dry matter intake, lb/d (kg/d) | 49.8 | (22.6) | 52.7 | (23.9) | 0.1 |
| Milk, lb/d (kg/d) | 26.7 | (12.1) | 28.4 | (12.9) | 0.46 |
| Milk, lb/d (kg/d) | 49.8 | (22.6) | 52.7 | (23.9) | 0.1 |

*Table 2. Hepatic lipidosis and incidence of disease.*

| Item | Control | ReaShure® | P Value |
|---|---|---|---|
| Hepatic Lipidosis [1], % | 40.5 | 14.3 | 0.05 |
| Subclinical ketosis [2], % | | | |
| 1 day postpartum | 37.2 | 28.5 | 0.070 |
| 14 day postpartum | 29.7 | 19.9 | 0.350 |
| Clinical Ketosis, % | 11.2 | 4.0 | 0.010 |
| Relapse of Ketosis, % | 6.8 | 2.3 | 0.050 |
| Mastitis, % | 22.5 | 14.7 | 0.060 |
| All postpartum diseases[3], % | 57.1 | 38.4 | 0.001 |

[1]Hepatic triglyceride > 5% wet tissue.
[2]Determined by measuring plasma beta-hydroxy butyric acid (lab test).
[3]includes retained placenta, metritis, clinical ketosis, displaced abomasum and mastitis.

## Conclusion

A significant body of evidence has accumulated to support choline as a required nutrient in transition cow diets. Supplementing transition cow diets with ReaShure® *Precision Release Choline* is a proven way to meet the transition dairy cow's dietary choline requirements by protecting choline from rumen degradation and delivering it to the small intestine for absorption. Adequate choline in the diet reduces liver fat accumulation, improved dry matter intake, increased milk yield and reduced the incidence of health disorders in the transition cow.

## References

Lima, F.S., M. F. Sá Filho, L. F. Greco, F. Susca, V. J. A. Magalhães, J. E. Garrett, and J. E. P. Santos. 2007. Effect of feeding rumen-protected choline (RPC) on lactation and metabolism. Journal of Dairy Science 90, 174 (Abstract).

Lima, F. S., M. F. Sá Filho, J. E. Garrett, and J. E. P. Santos. 2007. Effects of feeding rumen-protected choline (RPC) on health and reproduction of dairy cows. Journal of Dairy Science 90, 174 (Abstract).

Lima, F.S., B. A. Barton, and J.E.P. Santos. 2008. Feeding Rumen protected choline reduces the risk of hepatic lipidosis in transition dairy cows. Journal of Dairy Science 91, 219 (Abstract).

Lima, F. S., M. F. Sá Filho, L. F. Greco, and J.E.P. Santos. 2011. The Veterinary Journal. Volume 193, Issue 1, July 2012, Pages 140-145.

Santos, J.E. P. and F. S. Lima. 2009. Feeding rumen protected choline to transition dairy cows. Page 149 in proceedings of the Florida Nutrition Conference. Univ. Florida, Gainesville.

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Balchem Research Summary

# Effect of rumen-protected choline supplementation on liver and adipose gene expression during the transition period in dairy cattle

A study conducted by R. M. A. Goselink, J. van Baal, H. C. A, Widjaja, R. A. Deckker, R. L. G. Zom, M. J. de Veth, and A. M. van Vuuren. Wageningen UR Livestock Research, Netherlands. To be published in the February 2013 issue of the Journal of Dairy Science (currently on line at http://dx.doi.org/10.3168/jds.2012-5396).

## Background

During the transition period, hormonal changes and negative energy balance cause dramatic increases in fatty acid mobilization from adipose tissue, blood nonesterified fatty acid (NEFA) concentration, and uptake of NEFA by the liver. Ideally, NEFA are either completely oxidized to provide energy to the liver or are re-esterified to triglyceride (TG) and exported as a constituent of very low density lipoproteins (VLDL). The capacity of these metabolic pathways is exceeded during the transition period; consequently TG accumulates in the liver and ketone production from NEFA increases leading to fatty liver and subclinical or clinical ketosis. Research over the past decade (Cooke et al., 2007; Zom et al., 2011; Lima et al., 2012) has indicated that feeding ReaShure rumen-protected choline can reduce TG accumulation in the liver and incidence of ketosis. This probably occurs by alleviating a choline deficiency because unprotected choline in feeds is extensively degraded by microorganisms in the rumen. Fatty liver is a classic symptom of choline deficiency in nonruminant animals. In nonruminants, extensive research shows that choline is required for the synthesis of phophatidylcholine (PC), which in turn is required for VLDL assembly and secretion from the liver. The patho-physiology of fatty liver development during choline deficiency is presumed to be similar in nonrumininants and ruminants such as the transition dairy cow; however, it this has not been studied. Goselink et al. (2013) recently examined gene expression in liver and adipose tissue of control or ReaShure supplemented transition cows to provide insight into the mechanisms for reduction of liver TG.

## Trial Design

Sixteen multiparous Holstein Friesian dairy cows in good body condition (mean = 3.25) and not experiencing subclinical ketosis were fed 60 g ReaShure/day or a control diet from 3 weeks prior to calving until 6 weeks postcalving. This dose of ReaShure provides 15 g/day of choline in a form that is protected from degradation in the rumen. Cows were paired according to parity and expected calving date, and cows within each pair were randomly assigned to treatment. Cows were housed in groups and transponder-controlled feeders were used to dispense 582 g soybean meal and 18 g palm oil per day to control cows and 540 g soybean meal and 60 g ReaShure per day to treatment cows. In addition to these treatments, a dry cow feed mixture (grass silage/corn silage/wheat straw/soybean meal/premix) was consumed ad libitum and cows were gradually increased up to 2 lb of additional concentrate per day prior to calving. After calving, treatments continued and cows consumed a lactating cow feed mixture (grass silage/corn silage/grass seed straw/soybean meal/premix) ad libitum and were gradually increased from 2 to 17 lb of additional concentrate per day. Liver and adipose tissue were sampled at 3 weeks prior to calving and at 1, 3, and 6 weeks postpartum. Gene expression of key enzymes involved in fatty acid and energy metabolism were measured.

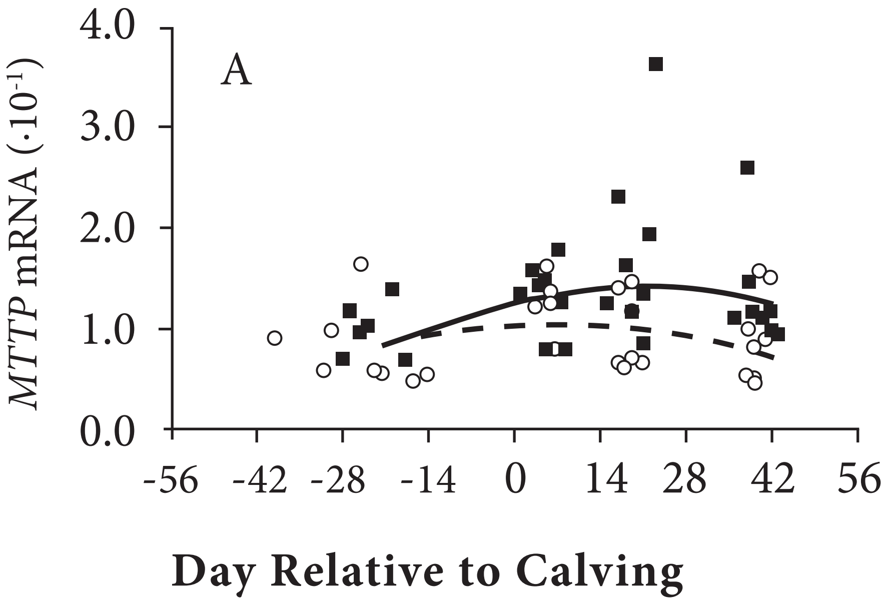
## Results and Discussion

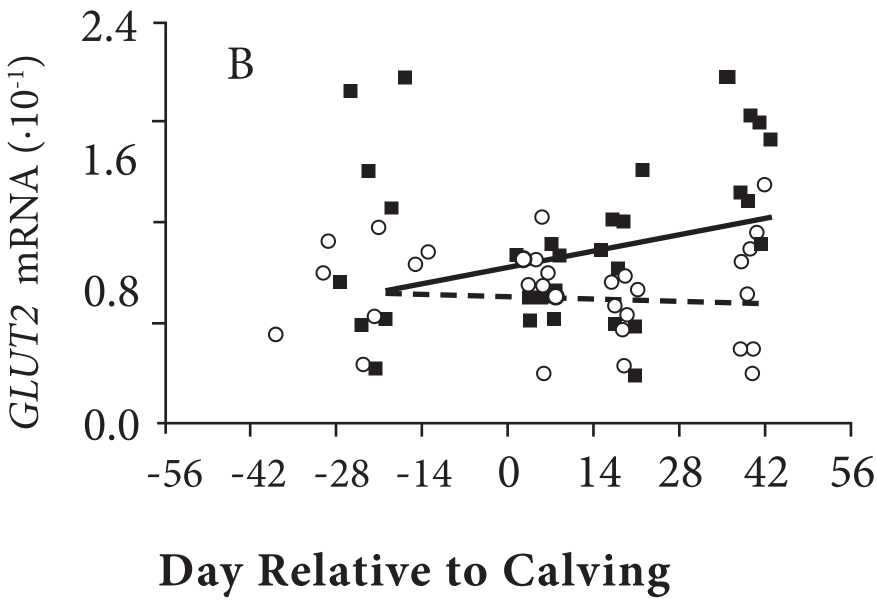
Effects of feeding ReaShure on feed intake, milk production and composition, blood metabolites, and liver TG from this trial were previously published (Zom et al., 2011). ReaShure significantly reduced liver TG at 1 and 4 weeks postpartum.

Feeding ReaShure did not affect adipose tissue gene expression of enzymes controlling lipolysis (Goselink et al., 2013) which suggests that choline does not influence liver TG levels by reducing fatty acid mobilization from adipose tissue and subsequent NEFA uptake by the liver. Cows fed ReaShure showed greater gene expression of liver microsomal TG transfer protein (MTTP; Figure 1). MTTP functions at the endoplasmic reticulum of the liver cell and is required for packaging TG into a VLDL and secreting it from the liver. The elevated MTTP suggests that supplementing choline facilitates TG export out of the liver and helps the transition cow cope with elevated NEFA uptake by the liver. Choline supplementation increased liver gene expression of apolipoprotein B100, a constituent of VLDL that is also required for VLDL secretion. This also suggests that VLDL TG export is enhanced when improving the choline status of transition cows. Although expression of genes involved in PC synthesis was not measured in this study, increased PC synthesis possibly could have been involved in triggering the expression of genes coding for MTTP and apolipoprotein B100 synthesis.

Interestingly, expression of genes (e.g. GLUT2; Figure 1) related to glucose production was also affected by feeding ReaShure. Previous research indicated ReaShure increases glucose storage as glycogen in the liver (Piepenbrink and Overton, 2003) and liver cells with lower TG content have higher rates of glucose synthesis (Strang et al., 1998). Ruminants absorb very little glucose from the gastro-intestinal tract and are highly dependent on the liver to synthesize glucose. Glucose is the precursor for lactose synthesis by the mammary gland. Lactose production is the primary determinant for volume of milk produced.

*Figure 1. ReaShure supplementation (solid line=RPC; dotted line=control) enhances expression of MTTP, a gene involved in VLDL assembly and secretion (panel A) and GLUT2, a gene involved in carbohydrate metabolism (Panel B).*




## Conclusions

Substantial evidence indicates that feeding ReaShure affects transition cows at the "whole animal" level, i.e., milk production, health, and reproduction (Oelrichs et al., 2004; Grummer, 2012; Lima et al., 2012). Additionally, previous research indicates that feeding ReaShure affects transition cows at the "organ" level, i.e., reduces liver fat during the transition period and negative energy balance (Cooke et al., 2007; Zom et al., 2011). The current study from Wageningen UR Livestock Research provides the first evidence that feeding ReaShure affects transition cows at the "molecular level". The effects observed at the molecular level are very consistent with previous observations at the organ or whole animal level. Choline-enhanced expression of genes involved in VLDL assembly and secretion correlates with lower liver TG content; alteration of genes involved with carbohydrate metabolism correlates with higher liver glycogen content and enhanced milk production.

## References


Cooke, R. F., N. Silva Del Rio, D. Z. Caraviello, S. J. Bertics, M. H. Ramos, and R. R. Grummer. 2007. Supplemental choline for prevention and alleviation of fatty liver in dairy cattle. J. Dairy Sci. 90: 2413-2418.

Goselink, R., J. van Baal., A. Widaja, R. Dekker, R. Zom., M. J. de Veth, and A. van Vuuren. 2013. Regulation of hepatic triacylglycerol level in dairy cattle by rumen-protected choline supplementation during the transition period. J. Dairy Sci. 96:(http://dx.doi.org/10.3168/jds.2012-5396).

Grummer, R. R. 2012. Choline: A limiting nutrient for transition dairy cows. Pages 22-27 in Proc. Cornell Nutr. Conf. Cornell University, Syracuse, NY.

Lima, F.S., M.F. Sa Filho, L. F. Creco, and J. E. P. Santos. 2012. Effects of feeding rumen-protected choline on incidence of diseases and reproduction in dairy cows. Vet. J. 193:140-145.

Oelrichs, W. A., M. C. Lucy, M. S. Kerley, and J. N. Spain. 2004. Feeding soybeans and rumen-protected choline to dairy cows during the periparturient period and early lactation. 2. Effects on reproduction. J. Dairy Sci. 87(Suppl. 1):344.

Piepenbrink, M. S., and T. R. Overton. 2003. Liver metabolism and production of cows fed increasing amounts of rumen-protected choline during the periparturient period. J. Dairy Sci. 86:1722-1733.

Strang, B. D., S. J. Bertics, R. R. Grummer, and L. E. Armentano. 1998. Effects of long-chain fatty acids on triglyceride accumulation, gluconeogenesis, and ureagenesis in bovine hepatocytes. J. Dairy Sci. 81:728-739.

Zom, R. L. G, J. van Baal, R. M. A. Goselink, J. A. Bakker, M. J. deVeth, and A. M. van Vuuren. 2011. Effect of rumen-protected choline on performance, blood metabolites, and hepatic triacylglycerols of periparturient dairy cattle. J. Dairy Sci. 94:4016-4027.



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Balchem Research Summary

# Effects of supplementation with ruminally-protected choline on performance of multiparous Holstein cows did not depend upon prepartum intake of calories

Zenobi, M., R. Gardinal, J. Zuniga, A. Dias, C. Nelson, J. Driver, B. Barton, J.E. Santos, and C. Staples. 2017. J. Dairy Sci. In Press.

## Introduction

Choline is an essential nutrient that enables cows to utilize the fat (NEFA) mobilized from body stores. The production of NEFA is the cows' natural way of managing negative energy balance during the early stages of lactation and is a primary source of energy for many functions. A healthy and properly functioning liver allows cows to transition smoothly, resulting in elevated peak milk and a more persistent lactation curve for maximum productivity. Issues occur when the cow's liver cannot effectively process all the NEFA being mobilized. This can adversely affect liver function, leading to increased ketones in the blood (ketosis). Ketosis can negatively affect feed intake and further exacerbate negative energy balance, leading to even more NEFA mobilization.

One aspect of this University of Florida study evaluated the impact of feeding ReaShure® *Precision Release Choline* to cows during the transition period on milk production over the entire lactation. The study also tracked cow health, reproduction, calf performance and colostrum quality.

## Experimental Design

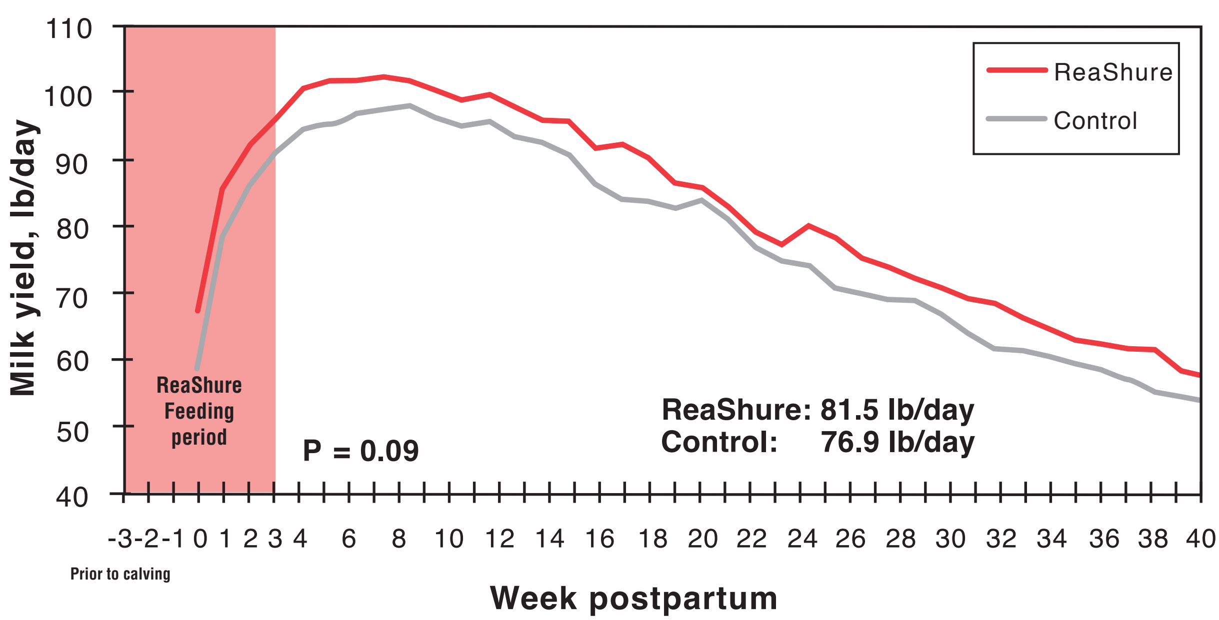
Ninety-three multiparous Holstein cows were assigned to one of four treatments at dry off. Treatments were dry cow diets that were formulated for either maintenance energy (0.64 Mcal NEL/lb) or high energy (0.74 Mcal NEL/lb) and then either with or without 60 grams of ReaShure for approximately 21 days prepartum through 21 days postpartum. After calving all cows received the same lactation diet and individual dry matter intakes and milk production was measured through 15 weeks of lactation.

## Results

***Increased Milk and Components over the 40-Week Lactation.***

Cows fed ReaShure during the transition period produced an average of 4.6 lbs more milk per day (P = 0.09) over the first 40-weeks postpartum (Figure 1). This calculates to an additional 1,288 lbs during the first 40 weeks of lactation. If we extrapolate these results over a 305-day lactation, the outcome would be an additional 1,403 lbs of milk per cow per year. Percent fat and protein were not statistically impacted for the ReaShure-fed cows. But both fat, 3.43 vs. 3.61 lbs/day (P = 0.09) and protein, 2.66 vs. 2.79 lbs/day (P = 0.07) yield increased as a result of the increased milk production seen in the ReaShure-fed cows. It is also of interest to note that cows (n = 76) considered to have non-excessive body condition at calving (BCS ≤ 3.5) produced on average 6.0 lbs more milk per day (P = 0.09) when fed ReaShure. This simply shows that cows of normal body condition respond quite well to ReaShure.

*Figure 1* Effect of Feeding ReaShure During Transition on Milk Production Over 40 Weeks



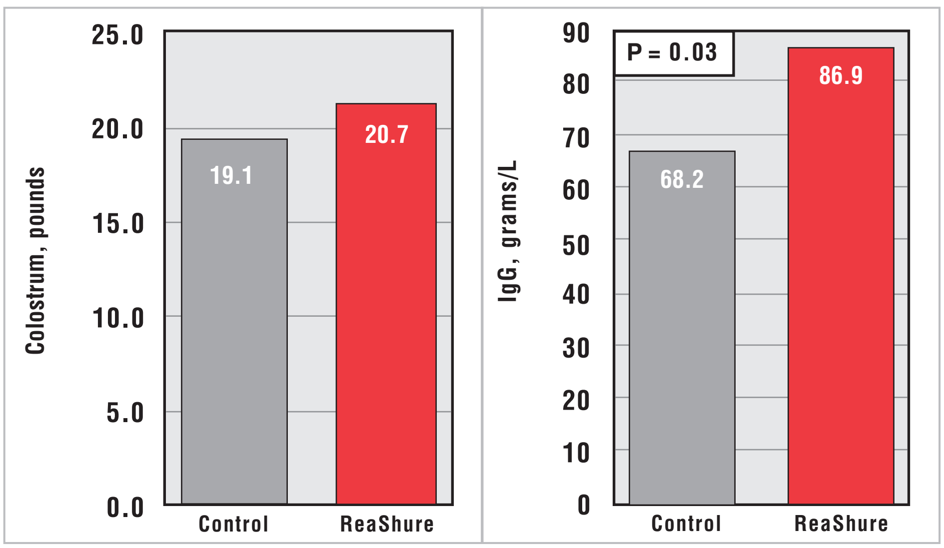
### *ReaShure and Health*

The authors noted in this study that there were not enough animals to effectively evaluate the effect of ReaShure on the incidence of diseases. Previous studies showed significant differences in clinical and subclinical ketosis but no differences were seen in this study. One very interesting and unexpected outcome in this study was a reduction ($P < 0.01$) in the prevalence of subclinical hypocalcemia (25.5 and 10.5%) as determined by total plasma calcium levels below 8.0 mg/100 ml at 0, 1, 3 or 7 days-in-milk. The mode of action for this is unclear at this time and will be studied in subsequent research trials.

### *Higher Quality Colostrum*

Colostrum volumes were statistically the same (19.1 vs. 20.7 pounds for the control and ReaShure fed cows, respectively). However, the ReaShure fed cows produced significantly ($P = 0.03$) more Immunoglobulin G per liter of colostrum (68.2 vs. 86.9 g/L, Figure 2). This could have practical implications for calf health.

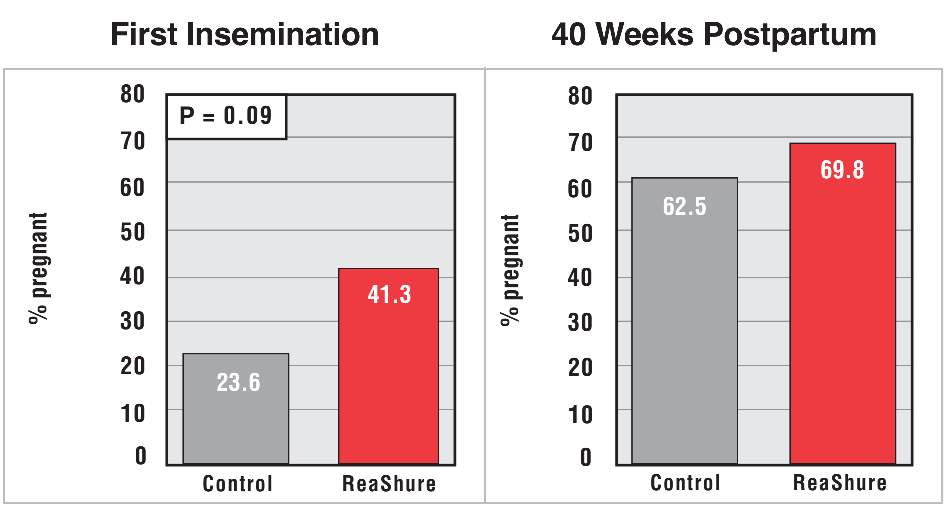
*Figure 2* Effect of Feeding ReaShure Prepartum on Colostrum Quantity and Quality




### *Improved Reproduction*

Pregnancies from first service were higher ($P = 0.09$) for cows fed ReaShure as compared to cows that were not (41.3 vs. 23.6%, Figure 3). While the ReaShure cows become pregnant more quickly, there was no significant difference in pregnancy rate by 40 weeks.

*Figure 3* Effect of Feeding ReaShure During Transition on Reproduction



***Calf Performance***

Researchers in this study followed the performance of heifer calves out to one year of age. Heifers born to the cows receiving ReaShure during the close-up dry period tended to be slightly smaller at birth than calves from control cows (Table 1). However, by 50 weeks of age heifers from cows fed ReaShure were significantly larger (P = 0.05) than those from cows not fed ReaShure during the close-up dry period. Average daily gain of heifers whose dam was fed ReaShure during the close-up dry period was 1.86 pounds per day which was 0.09 pounds per day faster than heifers from dams not fed ReaShure (P = 0.06).

## Summary

This study is consistent with previous peer-reviewed ReaShure research that demonstrated improvements in health and production parameters during and immediately following the transition period. However, this is the first study to measure the impact of feeding ReaShure on milk production over the entire lactation.

Cows receiving ReaShure during the transition period (21 days prepartum to 21 days postpartum) produced more milk per day over the 40-week lactation, had a lower prevalence of subclinical milk fever, showed improvements in first service conception rates, produced more immunoglobulin G in the colostrum and their heifer calves grew significantly faster through one year of age.

*Table 1* Effect of In Utero Exposure to ReaShure on Calf Performance

| Variable | Control | ReaShure | P Value |
|---|---|---|---|
| **Body Weight, lb** | | | |
| Calving | 89.0 | 84.4 | 0.07 |
| Weaning | 168.8 | 170.2 | 0.80 |
| 50 wk of age | 710.0 | 738.0 | 0.05 |
| **ADG (lb/d)** | | | |
| From calving to weaning | 1.34 | 1.38 | 0.67 |
| From weaning to 50 weeks | 1.87 | 1.96 | 0.05 |
| From calving to 50 weeks | 1.77 | 1.86 | 0.06 |

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# Give fresh cows that extra boost

What goes into the cow before it calves impacts both health and production in the subsequent lactation.

*by Marcos Zenobi, Jose Santos, and Charlie Staples*

ALL dairy cows mobilize stored fat for at least three weeks after calving to help support milk production. Metabolic problems such as ketosis and fatty liver are common during this time if cows struggle to use the mobilized fat efficiently, and that can take a toll on farm profits. Various strategies during the dry period have been proposed to help minimize inefficient fat utilization around calving. Controlling body condition at calving to a range of 3 to 3.5 is one such strategy because fat cows perform poorly. However, cows may store fat in their viscera (kidney and intestines), which is invisible to those who are body scoring cows.

Just as belly fat ("pot belly") in people has been linked to diabetes and heart disease, cows that accumulate belly fat during the dry period may be more prone to metabolic problems after calving. For many years, pregnant dry cows have been fed diets above their energy requirements, especially during the close-up period, in order to prepare the ruminal microbes for high-energy diets after calving and to compensate for reduced feed intake during the last one to two weeks of gestation. These diets are often heavy in corn silage or grain.

In some instances, dry cows are ignored and do not receive enough groceries resulting in under-condition at calving and lack the energy reserves to support milk in the early weeks. Alternatively, feeding diets that include less corn silage and more low-energy forages such as wheat straw may be "just right." These "just right" diets (Goldilocks diets) allow cows to eat as much as they want without gaining much weight.

**Performance after calving***

| | Calorie intake during the dry period | |
|---|---|---|
| Average for 15 weeks after calving | Excess ration | Maintenance ration |
| Dry matter intake, lbs./day** | 50.5 | 53.0 |
| Milk, lbs./day | 91.9 | 95.1 |
| Milkfat, % | 3.87 | 3.78 |
| Milk true protein, % | 2.95 | 2.97 |
| Energy balance for first five weeks, Mcal/day** | -8.7 | -3.6 |
| Liver fat for first three weeks, % of liver DM** | 10.6 | 8.5 |

*Both cow groups averaged 3.5 body condition score at calving.
**Cows fed different amounts of calories during the dry period performed differently postpartum (P<0.05).

## Exploring the Goldilocks diet

At the University of Florida, 93 multiparous Holstein cows were divided into two groups and fed one of two total mixed rations (TMRs) from dry-off to calving, spanning approximately seven weeks. One diet was 58 percent corn silage and 8 percent wheat straw (excessive intake of calories) whereas the second diet was 37.5 percent wheat straw, 23 percent corn silage, and 6 percent triticale silage (evenly balanced, the Goldilocks diet). Wet brew, citrus pulp, canola meal, and minerals/ vitamins were the other feed ingredients in both diets.

At two weeks before calving, cows offered the high corn silage diet ate more TMR dry matter (27.3 versus 24.7 pounds) and more energy (140 versus 109 percent of their energy requirement) compared to the high wheat straw "Goldilocks" group. Interestingly, during the last two weeks of gestation, cows fed the high corn silage diet dropped in feed intake twice as fast compared to the cows receiving the high straw diet. This rapid drop may predispose cows to metabolic problems upon calving.

Body condition score averaged 3.5 at the time of calving and did not differ between the two groups of cows. Cows were fed the same TMR postpartum (45 percent corn silage, 14



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percent ground corn, 15 percent soybean meal, 8 percent soybean hulls, 8 percent whole cottonseeds, 6 percent citrus pulp, and 4 percent minerals/vitamins). Cows were monitored closely for the first 15 weeks after calving.

Cows fed the "Goldilocks" diet prepartum ate on average 2.6 more pounds of TMR dry matter daily throughout the first 15 weeks following calving (53.1 versus 50.5 pounds per day). The "Goldilocks" cows eating more feed also produced 3.1 pounds per day more milk (95 versus 91.9 pounds per day), but this advantage was not statistically greater. Thus, cows eating the lower energy diet prepartum relied less on body energy reserves postpartum to sustain milk production.

During the first weeks postpartum, these cows were in less negative energy balance, had 10 percent less fat in their blood, exhibited fewer cases of ketosis, and had 20 percent less fat in their liver as determined from liver biopsies.

Overall, multiparous Holstein cows can be fed a single diet throughout the dry period that is matched to their nutrient requirements for pregnancy and maintenance that will result in a healthier and potentially more productive performance after calving.

## More milk possible

Another feeding strategy for pregnant dry cows is to add ruminally-protected choline (RPC) to the diet. Choline is a water-soluble vitamin found in feeds, but ruminal microbes destroy it during fermentation so that very little choline from the diet is available for absorption from the small intestine. The cow can synthesize some choline in its tissues, but apparently not enough to optimize milk production.

At the University of Florida, we fed 0 or 60 grams per day of an RPC product from 21 days before expected calving through 21 days after calving to 93 multiparous Holstein cows. Dietary methionine was maintained at 2.3 percent of metabolizable protein and the lysine to methionine ratio was 3:1.

Cows fed RPC tended to produce more milk (95.9 versus 91.1 pounds per day) without consuming more feed (52.5 versus 51.1 pounds per day) over the first 15 weeks of lactation. We continued to follow each cow's milk production after they went back into the general herd. Again, milk production tended to be greater over the first 40 weeks of lactation (81.8 versus 76.9 pounds per day).

Cows consuming RPC were in a more negative energy balance at two and three weeks after calving but without greater mean concentrations of plasma fatty acids or ketones (beta-hydroxybutyric acid) in the first five weeks. Liver fat (triacylglycerol) was also not higher in the RPC group during the first three weeks.

Choline has reduced fatty liver in many species, including dairy cows. In this experiment, it may have helped to prevent an increase in fatty liver in the midst of a temporary, more negative energy state.

## Choline helped health, too

For the first time, several additional benefits of feeding RPC were documented in our study. The prevalence of subclinical hypocalcemia (less than 8 milligrams of Ca/100 mL of plasma) was reduced from 25 to 10 percent during the first seven days postpartum when feeding RPC.

The immune status of the multiparous cows fed RPC appeared to be improved based upon 1) dropping rather than climbing rectal temperatures the first 12 days postpartum, 2) a greater proportion of the blood neutrophils killing bacteria at 17 days fresh, and 3) greater concentration and total production of immunoglobulins (IgG) in colostrum.

Using timed A.I. methods, pregnancy tended to be better (41.3 versus 23.6 percent; P less than 0.10) at first insemination (10 weeks postpartum) but did not differ by 40 weeks postpartum (69.8 versus 62.5 percent). From weaning to 12 months of life, heifers born from dams fed RPC had significantly better average daily gains (1.95 versus 1.85 pounds per day). Supplementing RPC for six weeks during transition, costing about $15 per cow, had long-term benefits for multiparous Holstein cows and replacement heifers.

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# Rumen-protected choline can aid transition cow health

*Choline plays a role in supporting liver health and milk production during the dairy cow's transition to the lactation period.*

By **HEATHER M. WHITE***

THE transition to lactation in the dairy cow's life cycle is a metabolically challenging period that reflects a coordinated response to calving and the onset of lactation.

Central to a successful transition period is the ability of the liver to make enough glucose to support milk production, specifically during a period characterized by reduced feed intake. When nutrition and metabolism cannot keep up with the demands of milk production, cows fail to reach their genetic potential for milk production and develop metabolic disorders such as ketosis and fatty liver.

Therefore, strategically feeding the transition dairy cow provides an opportunity to maximize milk production and improve metabolic health. While several nutrients and management strategies are key during this period, this review will focus on the role of choline in supporting liver health and milk production during the transition to the lactation period.

## Ketosis, fatty liver

Ketosis affects 40-60% of early-lactation dairy cows and costs an average of $289 per case (McArt et al., 2014). Ketosis — subclinical or clinical — results in decreased milk production, an increased risk of displaced abomasum and decreased reproductive efficiency (McArt et al., 2014).

Often developing alongside ketosis, fatty liver is defined as an accumulation of triacylglycerides in the liver, with clinical fatty liver defined as greater than 10% triacylglycerides on a wet weight basis (Bobe et al., 2004). Fatty liver is associated with decreased milk production, a decreased life span, increased veterinary costs and longer calving intervals and affects 60% of dairy cows (Drackley, 1999; Bobe et al., 2004).

Preventing ketosis and fatty liver is of great interest because metabolic disorders are a known contributor to involuntary culling in the first 30 days after calving, as well as to decreased milk production and impaired animal health.

Supplementing transition cows with rumen-protected choline was found to decrease cases of ketosis and relapse of ketosis after treatment (Lima et al., 2007). The incidence of mastitis and overall morbidity were also reduced in the cows supplemented with rumen-protected choline, which may reflect an improvement in immune function, as discussed later.

Supplementing transition dairy cows with rumen-protected choline decreased lipid accumulation in the liver (Cooke et al., 2007; Zom et al., 2011). This decrease in fatty liver was probably not due to decreased lipid mobilization since concentrations of non-esterified fatty acids (NEFAs) in the blood were the same as for non-supplemented cows; rather, it was likely due to increased very-low-density lipoprotein (VLDL) export from the liver and improved liver energy metabolism (Goselink et al., 2013).

Quantifying VLDL export from the liver was previously very challenging; however, with improved technology, it is now possible. VLDL export from the liver not only helps alleviate liver lipid accumulation, but it also provides a fatty acid source for the mammary to use for milk fat synthesis. While this is a great benefit, it makes it challenging to identify if more VLDL is being released from the liver in a lactating cow because the mammary gland may increase uptake at the same time, resulting in no net change in blood VLDL concentration.

To overcome this, experiments with bovine liver cells were used to measure VLDL package and export. Increased VLDL export was also observed when liver cells were supplemented with increasing concentrations of choline (McCourt et al., 2015). These *in vitro* experiments are important for isolating the mechanism of choline action and support choline's role in VLDL packaging and export from the cell.

As mentioned, the liver is responsible for generating glucose that is used by the mammary gland to make lactose for milk. For a high-producing dairy cow, the bovine liver can make 12-20 lb. of glucose each day, via gluconeogenesis, to support milk production. The precursor for glucose production is primarily propionate produced in the rumen; however, when feed intake is not adequate to support milk production, the glycerol backbone of mobilized fatty acids, lactate and amino acids are also used (Aschenbach et al., 2010; White et al., 2015).

During fatty liver, gluconeogenesis in the liver is impaired, resulting in a decreased supply of glucose to the mammary gland (Rukkwamsuk et al., 1999; Murondoti et al., 2004). This contributes to decreased milk production in cows with fatty liver (Bobe et al., 2004).

When all choline supplementation studies are analyzed together, they show an increase in milk production of almost 5 lb. per day (Grummer, 2015), which can likely be attributed to increased liver function and glucose production.

## Oxidative stress

Nutrition researchers are becoming more aware of the negative effects of inflammation and oxidative stress on liver function in dairy cows. The connection between the immune system and metabolism is seen when examining the relationship of co-morbidities such as ketosis, metritis and mastitis.

In cows that have early metritis, acute mastitis and chronic mastitis, the odds ratio of the cows later developing ketosis is between 1.5 and 2.5, compared to cows that didn't have one of the initial infections (Grohn et al., 1989). The reverse relationship is also well established, and when cows have ketosis, they have an increased risk of developing metritis (Duffield et al., 2009).

Inflammation influences many metabolic pathways, including mobilization of adipose tissue, the onset of insulin resistance and increased lipid deposition in the liver (Drackley, 1999; Kushibiki et al., 2001 and 2003; Ingvartsen, 2006; Bradford, 2011), and it may explain the development of multiple co-morbidities during the transition to the lactation period (Bradford, 2011).

In this light, the reduced incidence of mastitis and overall morbidity observed during supplementation of rumen-protected choline may be attributable to improved immune function.

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Pro-inflammatory cytokines, such as tumor necrosis factor-alpha (TNF-a), have many effects in the liver (reviewed by Bradford, 2011). In the liver, TNF-a can decrease glucose production and increase triglyceride storage of mobilized NEFAs. The increased lipid storage may be due to decreased fatty acid oxidation with TNF-a exposure and decreased production of apolipoproteins, which may impair VLDL export.

When cows are challenged directly with TNF-a, dry matter intake is reduced, and ketosis incidence is numerically increased from 9% to 27% (Yuan et al., 2013). While the decreased VLDL export during TNF-a challenge represents a different mechanism compared with choline deficiency (decreased apolipoproteins versus phosphotidylcholine, respectively), choline supplementation could potentially attenuate this negative effect through increasing VLDL export (McCourt et al., 2015) and increasing feed intake (Grummer, 2015).

Although further research is needed to elucidate this aspect of the choline mechanism, this could contribute to the reduction of metabolic disorders such as ketosis and fatty liver with choline supplementation.

In addition to inflammatory responses, there is also increased oxidative stress during the transition to the lactation period. Oxidation of fatty acids is critical for energy production in the liver; however, it also results in oxidative stress within the cells.

This is exacerbated when peroxisomal oxidation is increased in early lactation. Although this adaptation serves to increase the overall oxidative capacity, the first step of peroxisomal oxidation produces hydrogen peroxide and contributes to reactive oxygen species production (Grum et al., 1996; Drackley, 1999; Bradford, 2011).

Rumen-protected choline can reduce oxidative stress of the liver (Rahmani et al., 2014). This was further demonstrated in the cell culture model described previously in which increasing concentrations of choline tended to decrease reactive oxygen species released into the cell culture media (Chandler et al., 2015). This may suggest another aspect of the mechanism of choline action in the cow and could be one of the potential interventions to improving immune function in transition dairy cows.

## Conclusions

Both whole animal and cell culture experiments have been used to further the understanding of choline's role in liver health and function. The metabolic challenges associated with the transition to the lactation period in dairy cows lead to negative impacts on milk production, cow health, inflammation and oxidative stress.

## References


Aschenbach, J.R., N.B. Kristensen, S.S. Donkin, H.H. Hammon and G.B. Penner. 2010. Gluconeogenesis in dairy cows: The secret of making sweet milk from sour dough. IUBMB Life. 62:869-877.

Bobe, G., J.W. Young and D.C. Beitz. 2004. Invited review: Pathology, etiology, prevention and treatment of fatty liver in dairy cows. J. Dairy Sci. 87:3105-3124.

Bradford, B. 2011. The role of inflammation in metabolic disorders. Proceedings of the Mid-South Ruminant Nutrition Conference. p. 35-42.

Chandler, T.L., C.L. McCourt, S.J. Bertics, B.A. Barton and H.M. White. 2015. Methyl-donors choline and methionine differentially alter hepatic methyl carbon metabolism. J. Dairy Sci. Vol. 98, Suppl. 2.

Cooke, R.F., N. Silva del Rio, D.Z. Caraviello, S.J. Bertics, M.H. Ramos and R.R. Grummer. 2007. Supplemental choline for prevention and alleviation of fatty liver in dairy cattle. J. Dairy Sci. 90:2413-2418.

Drackley, J.K. 1999. ADSA Foundation Scholar Award. Biology of dairy cows during the transition period: The final frontier? J. Dairy Sci. 82:2259-2273.

Duffield, T.F., K.D. Lissemore, B.W. McBride and K.E. Leslie. 2009. Impact of hyperketonemia in early lactation dairy cows on health and production. J. Dairy Sci. 92:571-580.

Goselink, R.M.A., J. van Baal, H.C.A. Widjaja, R.A. Dekker, R.L.G. Zom, M.J. de Veth and A.M. van Vuuren. 2013. Effect of rumen-protected choline supplementation on liver and adipose gene expression during the transition period in dairy cattle. J. Dairy Sci. 96:1102-1116.

Grohn, Y.T., H.N. Erb, C.E. McCulloch and H.S. Saloniemi. 1989. Epidemiology of metabolic disorders in dairy cattle: Association among host characteristics, disease and production. J. Dairy Sci. 72:1876-1885.

Grummer, R.R. 2015. Choline: A limiting nutrient for transition dairy cows. Proceedings of the Florida Nutrition Conference.

Ingvartsen, K.L. 2006. Feeding- and management-related diseases in the transition cow: Physiological adaptations around calving and strategies to reduce feeding-related diseases. Anim. Feed Sci. Tech. 126(3-4):175-213.

Kushibiki, S., K. Hodate, H. Shingu, Y. Obara, E. Touno, M. Shinoda and Y. Yokomizo. 2003. Metabolic and lactational responses during recombinant bovine tumor necrosis factor-alpha treatment in lactating cows. J. Dairy Sci. 86:819-827.

Kushibiki, S., K. Hodate, H. Shingu, Y. Ueda, Y. Mori, T. Itoh and Y. Yokomizo. 2001. Effects of long-term administration of recombinant bovine tumor necrosis factor alpha on glucose metabolism and growth hormone secretion in steers. Am. J. Vet. Res. 62:794-798.

Lima, F.S., M.F. Sa Filho, L.F. Greco and J.E.P. Santos. 2012. Effects of feeding rumen-protected choline on incidence of diseases and reproduction of dairy cows. Vet. J. 193:140-145.

McArt, J.A.A., D.V. Nydam, G.R. Oetzel and C.L. Guard. 2014. An economic analysis of hyperketonemia testing and propylene glycol treatment strategies in early lactation dairy cattle. Prev. Vet. Med. 117:170-179.

McCourt, C.L., T.L. Chandler, S.J. Bertics, B.A. Barton and H.M. White. 2015. Supplementation of choline increases very low-density lipoprotein export from bovine primary hepatocytes. J. Dairy Sci. Vol. 98, Suppl. 2.

Murondoti, A., R. Jorritsma, A.C. Beynen, T. Wensing and M.J.H. Geelen. 2004. Unrestricted feed intake during the dry period impairs the postpartum oxidation and synthesis of fatty acids in the liver of dairy cows. J. Dairy Sci. 87:672-679.

Rahmani, M., M. Dehghan-banadaky, R. Kamalyan, H. Malekinejad, F. Rahmani, M.H.H. Tavatori and H. Mohammadi. 2014. Effects of feeding rumen-protected choline and vitamin E on serum protein fractions, total thiol molecules and total antioxidant capacity in early lactating dairy cows. Global J. Anim. Sci. Res. 2:337-344.

Rukkwamsuk, T., T. Wensing and M.J. Geelen. 1999. Effect of fatty liver on hepatic gluconeogenesis in periparturient dairy cows. J. Dairy Sci. 82:500-505.

White, H.M. 2015. The role of TCA cycle anaplerosis in ketosis and fatty liver in periparturient dairy cows. Animals. 5:793-802.

Yuan, K., J.K. Farney, L.K. Mamedova, L.M. Sordillo and B.J. Bradford. 2011. TNF-alpha altered inflammatory responses, impaired health and productivity but did not affect glucose or lipid metabolism in early-lactation dairy cows. PLOS ONE. 8:e80316.

Zom, R.L.G., J. van Baal, R.M.A. Goselink, J.A. Bakker, M.J. de Veth and A.M. van Vuuren. 2011. Effect of rumen-protected choline on performance, blood metabolites and hepatic triacylglycerols of periparturient dairy cattle. J. Dairy Sci. 94:4016-4027. ■

# Choline gaining respect as an essential nutrient

*Choline is gaining notice for the growing list of important roles it plays in animal health and well-being. Choline recently was suggested as a requirement for transition dairy cattle.*

By **RIC GRUMMER***

HISTORICALLY, choline has been the Rodney Dangerfield of nutrients, getting seemingly little respect from much of the animal and human nutrition communities.

There probably are a variety of reasons for this, but perhaps the greatest is that nobody seems to know how to classify it. Choline is often referred to being "vitamin-like," but it does not belong to that fraternity because it is not an enzyme cofactor, it can be synthesized endogenously and it is fed in larger quantities than vitamins.

Structurally, choline is similar to an amino acid, but it is not a building block for protein synthesis. Functionally, one may like to lump it with lipids, but on its own, it definitely is not a lipid. Carbohydrate? Not even close.

Yet, choline was first isolated from pig bile in 1849, so it has been a known entity for more than 150 years. Choline's lipotropic effect was characterized in the 1920s and 1930s, and research in the 1940s and 1950s established it as a required nutrient for rats and chickens.

In 1998, the Institute of Medicine of the National Academies declared choline as an essential nutrient for people, and adequate intake values were defined. In March 2014, the U.S. Food & Drug Administration proposed a reference daily intake for choline, which allows it to be included on Nutrition Facts and Supplement Facts labels with an associated percent daily value.

Respected or not, it is impossible to ignore the growing list of important roles choline plays in animal health and well-being.

## Choline functions

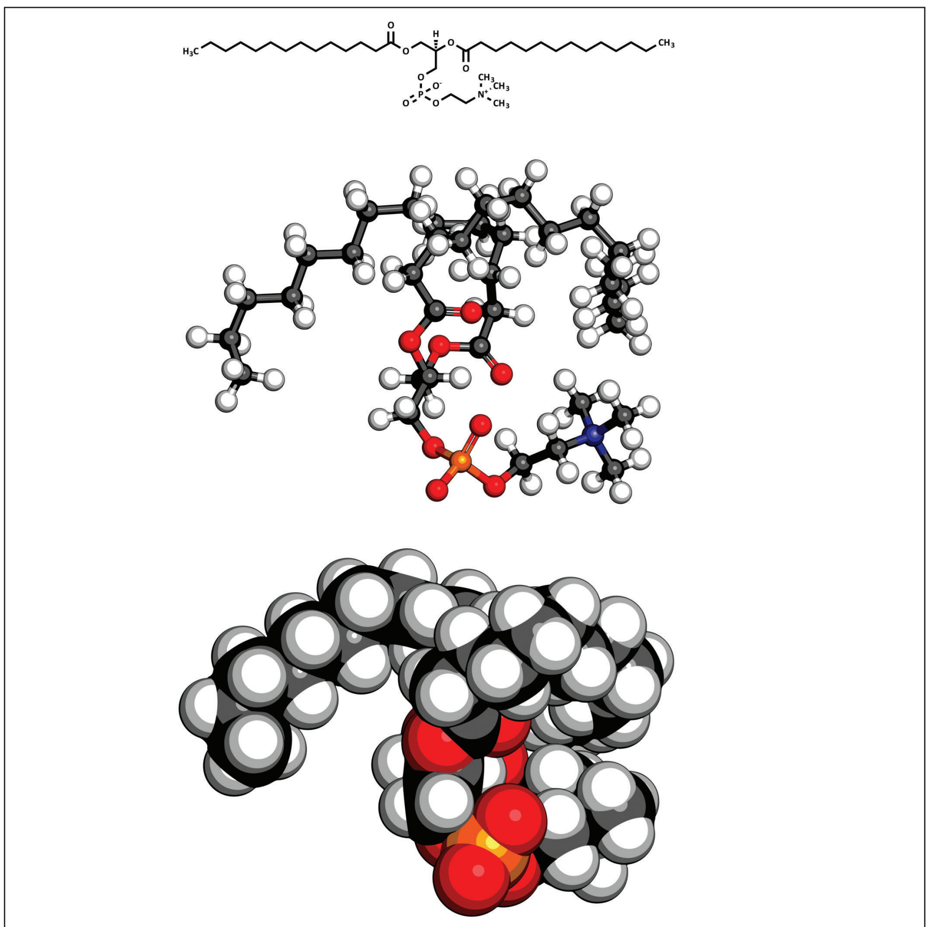
Many functions of choline have been well established for years. Choline is found in biological systems primarily as phosphatidylcholine (PC).

PC is an essential constituent of cell membranes, as is lysoPC, choline plasmalogen and sphingomyelin and other choline-containing compounds. PC is the predominant phospholipid (greater than 50%) in most mammalian membranes. As a component of milk fat globule membranes, choline is required for milk production.

PC can be derived from dietary choline or from endogenous synthesis by methylation of phosphatidylethanolamine. Endogenous synthesis of PC is critically important, especially in cattle, where ruminal destruction of choline is extensive.

PC is also a constituent of lipoproteins, including chylomicrons, low-density lipoproteins, very-low-density lipoproteins (VLDL) and high-density lipoproteins. Lipoproteins are instrumental in facilitating lipid transport between tissues via the blood stream.

Of particular importance is PC as a constituent of VLDL, which is synthesized in the liver and transports fat from the liver to muscle, adipose and mammary tissue. Several experimental models have shown that PC deficiency curtails VLDL export and leads to development of fatty liver



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**CHOLINE MOLECULE:** Shown is the phosphatidylcholine (PC) cell membrane building block molecule. Choline is found in biological systems primarily as PC.

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(more on this biology will be covered in part 2 of this series). This vital role of choline in hepatic metabolism explains why fatty liver is the classic deficiency symptom when diets do not deliver adequate choline for intestinal absorption.

Following irreversible enzymatic oxidation to betaine, methyl groups of choline can be used in many biochemical reactions. One of the most important is the synthesis of methionine via methylation of S-adenosylmethionine. Interestingly, the methyl group of methionine can also be used to synthesize choline as PC from phosphatidylethanolamine. This metabolic relationship suggests that choline absorbed from the diet may be able to spare some dietary methionine, and vice versa. This has been shown to be the case in several non-ruminant species; more research is needed to define this relationship in ruminants.

Structurally, choline contains three methyl groups, and methionine contains one. When adjusted for differences in molecular weight between choline and methionine, choline has 4.3 times more methyl groups than methionine. There may be interactions between choline and other nutrients involved with methyl transfer, e.g., folic acid. During the past 10 years, there has been considerable interest in the role of choline and other methyl donors in DNA methylation and gene expression. DNA methylation in the region of a gene is usually associated with expression being turned off.

Clearly, these findings open up an infinite array of possibilities by which choline may influence animal production, reproduction and health.

Considerable research during the past two decades has led to the Institute of Medicine and FDA recognizing the importance of choline for public health and the development of guidelines for intake.

While much of this research was conducted in lab animals and humans, it would be naive to think that choline does not play similar roles in domesticated animals. Exciting areas of research include the role of choline in pregnancy and lactation and cognitive function (Blusztajn, 1998; Zeisel and Costa, 2009).

Maternal reserves of choline are depleted during pregnancy and lactation. The fetus demands large quantities of choline, and the choline concentration in amniotic fluid is 10 times greater than in maternal blood. Inadequate intake of nutrients involved in methyl donation during early pregnancy, including choline, has been associated with greater birth defects of the brain, spine and/or spinal cord (Zeisel and Costa, 2009).

During later periods of pregnancy, when the hippocampus (memory center) is developing, the choline status of pregnant rodents has been shown to affect the brain structure and function of their newborns, as measured by cognitive or behavioral tests (Zeisel, 2000; McCann et al., 2006).

Similar results have been observed in newborn rats when their mothers' diet was supplemented with choline. Interestingly, adult rodents exposed to extra choline while *in utero* showed a reduced decline in memory as they aged and enhanced auditory and visual responses (Zeisel, 2004). This suggests that the choline status of the pregnant mother has long-term implications for the offspring's memory enhancement.

Choline supplementation in adult rats also improves spatial memory capacity and precision (Meck et al., 1988; Meck et al., 1989).

Evidence indicates that choline supplementation in long-term total parenteral nutrition patients leads to improved visual memory in the elderly and improved neuropsychological development in children (Buchman et al., 2001).

The mechanism of action for these observations is largely unknown, but several possibilities exist (Blusztajn, 1998; Zeisel, 2000; Zeisel, 2006).

Choline appears to influence the rate of birth and death of nerve cells in the developing hippocampus. Choline's role as a precursor for the synthesis of acetylcholine, an important neurotransmitter, has been implicated. DNA methylation and changes in gene expression in stem cell proliferation and differentiation may be involved. Cognitive decline during aging has been linked to oxidative stress and high blood concentrations of homocysteine, which are inversely related to blood choline concentrations.

## Choline sources

For people, animal products are the best source of choline. Eggs are the richest source of choline because of the large content of PC in the yolk. Liver and milk are also excellent sources of choline. Consuming one egg per day would increase the percentage of pregnant women who get adequate choline intake from 10% to more than 50%.

For domesticated non-ruminant animals, oilseeds and their meals (cottonseed, soybean and sunflower) are among the richest sources of choline. Fish meal is also an excellent source. Choline can be supplemented to non-ruminant diets as choline chloride.

Feed sources of choline and choline chloride are extensively degraded in the rumen of beef and dairy cattle. If choline chloride is supplemented to ruminant diets, it must be in a form that is protected from ruminal degradation.

## Final thoughts

An essential nutrient is one required for normal body functioning that either cannot be synthesized by the body at all or cannot be synthesized in amounts adequate for good health. Consequently, it must be obtained by a dietary source.

Similar to many nutrients, the essentiality of choline was first established by animal nutrition researchers working with non-ruminant animals, including swine and poultry. Recently, choline was suggested as a requirement for transition dairy cattle, which is logical because they exhibit the classic deficiency symptom (fatty liver) and, as ruminants, have extensive degradation of dietary choline.

In recent years, the human nutrition and medical community has recognized choline as an essential nutrient for brain function and memory, and this has served as a stimulus for exciting new research that has led to novel discoveries on the importance of adequate choline intake for optimal health and well-being. While choline may not belong to any traditional nutrient classification (e.g., vitamins), one can certainly agree that it is a "vital amine" (Blusztajn, 1998).

## References


Blusztajn, J.K. 1998. Choline, a vital amine. Science 281:794-795.

Buchman, A.L., M. Sochel, M. Brown, D.J. Jenden, C. Ahn, M. Roch and T.L. Brawley. 2001. JPEN J. Parenter. Enteral Nutr. 25:30-35.

Mcann, J.C., M. Hudes and B.N. Ames. 2006. An overview of evidence for a causal relationship between dietary availability of choline during development and cognitive function in offspring. Neurosci. Biobehav. Rev. 30:696-712.

Mech, W.H., R.A. Smith and C.L. Williams. 1988. Pre- and postnatal choline supplementation produces long-term facilitation of spatial memory. Dev. Psychobiol. 21:339-353.

Mech, W.H., R.A. Smith and C.L. Williams. 1989. Organizational changes in cholinergic activity and enhanced visuospacial memory as a function of choline administered prenatally or postnatally or both. Behav. Neurosci. 103:1234-1241.

Zeisel, S.H. 2000. Choline: Needed for normal development of memory. J. Am. Coll. Nutr. 19(5 Suppl.):528S-531S.

Zeisel, S.H. 2004. Nutritional importance of choline for brain development. J. Am. Coll. Nutr. 23(6 Suppl.):612S-626S.

Zeisel, S.H. 2006. The fetal origins of memory: The role of dietary choline in optimal brain development. J. Pediatr. 149(5 Suppl.):S131-136.

Zeisel, S.H., and K. Costa. 2009. Choline: An essential nutrient for public health. Nutr. Rev. 67:615-623. ■

# Choline aids fat metabolism in transition dairy cows

*Rumen-protected choline supplementation in the dairy transition period may improve fatty acid transport and processing.*

By **ROSELINDE M.A. GOSELINK** and **HEATHER M. WHITE***

THE transition period is a very sensitive and essential period for dairy cows. Many metabolic and infectious diseases originate during the transition period, causing a cascade of trouble in dairy cattle that easily results in involuntary culling.

The transition period, therefore, holds the key to improving not just dairy cow health and performance but also dairy cow welfare, longevity and farm profitability (Van Knegsel et al., 2014).

## Transition dairy cattle

Today's dairy cow is a metabolic acrobat during the transition period. She manages, in just a couple of days, to shift her physiological status from the relatively lazy life of a dry cow to the high metabolic activity needed for milk production while also giving birth to a calf.

Milk production has an extremely high metabolic priority in early lactation, often requiring in excess of 4 lb. of glucose for lactose production each day. The drive for milk production also pushes the mobilization of the mother's body reserves (adipose and muscle) to be utilized for milk output, all for evolutionary reasons: ensuring the survival of her offspring.

The dairy industry has actually been exploiting this mammalian trait in past decades via genetic selection for milk production. Peak production in early lactation largely depends on the capacity to mobilize body reserves, so the current dairy cow has become an excellent fat mobilizer.

During this acrobatic masterpiece, there is a thin line of distinction between a successful transition and developing transition disorders. The dairy cow needs a safety net of adequate management and nutrition to reduce metabolic stress and the risk of disease. Mobilization and processing of fat is an important factor for success. Thus, there is a need to understand and support the dairy cow's fat metabolism in the transition period.

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## Fatty acid traffic

Fat mobilization is stimulated by periods of low energy intake but also directly by the hormonal changes in early lactation to support milk production. In this process, the adipose tissue is stimulated to degrade stored triglycerides to non-esterified fatty acids (NEFAs) and a glycerol backbone. These NEFAs are released into the bloodstream and transported to the liver, where they may be directed toward different metabolic pathways.

Since fatty acids are energy-rich nutrients, the first option for processing NEFAs in the liver is oxidation to provide energy to maintain and support liver function. If NEFA input is higher than the liver's energy requirement, partial oxidation will result in the production of ketone bodies — e.g., beta-hydroxybutyric acid (BHBA) — that are released into the bloodstream.

The BHBAs released are not wasted; they can be used as an energy source in organs other than the liver, such as muscle, the mammary gland or the brain. However, if BHBA concentrations in the blood rise above 1.2 mmol per liter, the cow is considered to have (sub)clinical ketosis (LeBlanc et al., 2010).

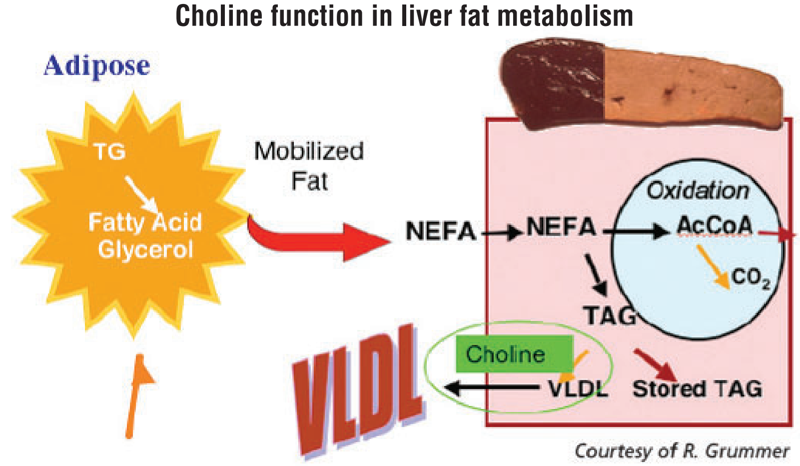
These high circulation levels of BHBA have a negative effect on feed intake and increase the risk for other diseases and early culling (Laeger et al., 2013; McArt et al., 2012; LeBlanc, 2010).

In addition to oxidation, another option for NEFA processing in the liver is the recombination of NEFA with glycerol to form triacylglycerol (TAG). These TAG molecules are exported to various organs after being secreted into the bloodstream with a hydrophilic envelope of protein, cholesterol and phospholipids.

This TAG carrier system is called very-low-density lipoprotein (VLDL) transport. The VLDL particles released into the bloodstream can dock at the udder to deliver triglycerides for milk fat synthesis or at other organs that can use some NEFA for energy production. However, if VLDL transport components (like protein or phospholipids) are limiting, TAG cannot be exported. If NEFA uptake by the liver is too high, TAG will accumulate, resulting in fatty liver disease.

This intracellular fat accumulation may

**Choline function in liver fat metabolism**




TG = triglycerides
AcCoA = acetyl coenzyme A
NEFA = non-esterified fatty acids
VLDL = very-low-density lipoprotein
TAG = triacylglycerol

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interfere with normal liver metabolism, thus increasing the risk for other metabolic and infectious diseases (which will be discussed in part 3 of this series).

## Role of choline

Choline is part of phosphatidylcholine, one of the major phospholipids required for VLDL transport. It can be synthesized by the animal itself using methyl donors, such as the essential amino acid methionine, or directly from absorption of dietary choline. In early lactation, however, endogenous synthesis from methyl donors seems to be insufficient to meet the demand for VLDL export.

Unfortunately, dietary choline is rapidly degraded by microorganisms in the rumen. To support choline requirements, supplemental choline needs to be protected against ruminal degradation. Supplementation of rumen-protected choline has been shown to be effective in reducing the TAG concentration in the liver during the transition period (Zom et al., 2011).

The Figure shows the process of fatty acid mobilization and transport and the role of choline.

To investigate the mode of action of choline in the transition period, "nutrigenomics" can be applied. Nutrigenomics is the study of the effect of nutrients like choline on gene expression in any tissue of interest.

Increased expression of genes encoding for a certain metabolic pathway helps demonstrate which metabolic processes are stimulated by choline supplementation. Analyzing liver biopsies of dairy cattle with and without rumen-protected choline supplementation, the supplemented cows showed an increased expression of genes encoding for fatty acid transport and VLDL assembly (Goselink et al., 2013). This confirms the idea that choline helps stimulate VLDL export of TAG from the liver (Figure).

Demonstrating that supplemental rumen-protected choline enhances the export of VLDL from the liver in animals is challenging for two reasons: (1) differences in composition (compared to other animals) make it technically difficult to distinguish VLDL from other forms of lipid transport moieties, and (2) any potential increase in blood VLDL concentration from enhanced liver export may be masked by increased uptake of VLDL by the udder or other tissues.

To overcome these obstacles, cell culture models recently were used to examine the role of choline and methionine in liver cells and VLDL export. These studies demonstrated that choline, but not methionine, increased the export of VLDL when liver cells were challenged with NEFA concentrations similar to those experienced by transition dairy cows (McCourt et al., 2015). The study also highlighted the important yet different roles choline and methionine play in liver function (Chandler et al., 2015).

Together with research in transition cows, these findings support supplementing choline during transition from the dry period to lactation to optimize liver function.

## Conclusions

Fat mobilization in the transition period is a normal physiological process for mammalian species. With the high milk and mobilization potential of modern dairy cows, fat metabolism needs to be managed to prevent excessive partial oxidation of NEFA and TAG accumulation in the liver.

Rumen-protected choline supplementation during this critical period may specifically improve fatty acid transport and processing, thereby preventing metabolic disease and other maladies.

## References

Chandler, T.L., C.L. McCourt, S.J. Bertics, B.A. Barton and H.M. White. 2015. Methyl-donors choline and methionine differentially alter hepatic methyl carbon metabolism. J. Dairy Sci. Vol. 98, Suppl. 2.

Goselink, R.M.A., J. van Baal, H.C.A. Widjaja, R.A. Dekker, R.L.G. Zom, M.J. de Veth and A.M. van Vuuren. 2013. Impact of rumen-protected choline supplementation on liver and adipose gene expression during the transition period in dairy cattle. J. Dairy Sci. 96:1102-1116.

Laeger, T., H. Sauerwein, A. Tuchscherer, O. Bellmann, C.C. Metges and B. Kuhla. 2013. Concentrations of hormones and metabolites in cerebrospinal fluid and plasma of dairy cows during the periparturient period. J. Dairy Sci. 96:2883-2893.

Leblanc, S. 2010. Monitoring metabolic health of dairy cattle in the transition. J. Reprod. Dev. 56:S29-S35.

McArt, J.A.A., D.V. Nydam and G.R. Oetzel. 2012. Epidemiology of subclinical ketosis in early lactation dairy cattle. J. Dairy Sci. 95:5056-5066.

McCourt, C.L., T.L. Chandler, S.J. Bertics, B.A. Barton and H.M. White. 2015. Supplementation of choline increases very low-density lipoprotein export from bovine primary hepatocytes. J. Dairy Sci. Vol. 98, Suppl. 2.

Van Knegsel, A.T.M., H.H. Hammon, U. Bernabucci, G. Bertoni, R.M. Bruckmaier, R.M.A. Goselink, J.J. Gross, B. Kuhla, C.C. Metges, H.K. Parmentier, E. Trevisi, A. Troscher and A. Van Vuuren. 2014. Metabolic adaptation during early lactation: Key to cow health, longevity and a sustainable dairy production chain. CAB Reviews 9.

Zom, R.L.G., J. van Baal, R.M.A. Goselink, J.A. Bakker, M.J. de Veth and A.M. van Vuuren. 2011. Effect of rumen-protected choline on performance, blood metabolites and hepatic triacylglycerols of periparturient dairy cattle. J. Dairy Sci. 94:4016-4027. ■