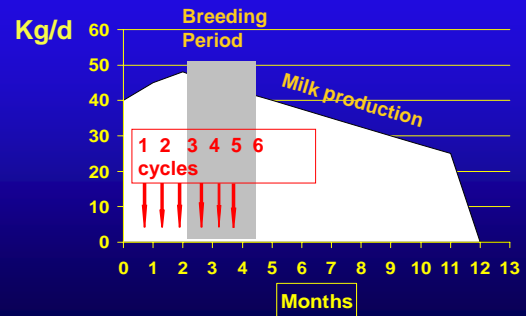
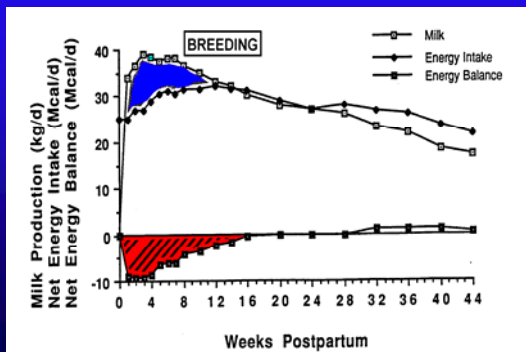


## Understanding and using MUNs

## Milk Production and Reproduction



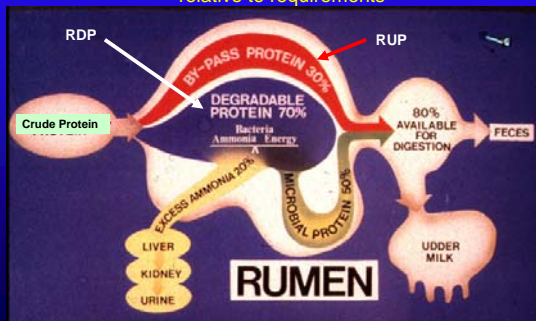
## Negative energy balance in early lactation decreases fertility



## High protein diets support high milk production, but increase plasma urea in association with lower fertility



Protein metabolism- the biological value of dietary protein is directly related to the energy status of the lactating dairy cow and the balance of absorbed AA relative to requirements



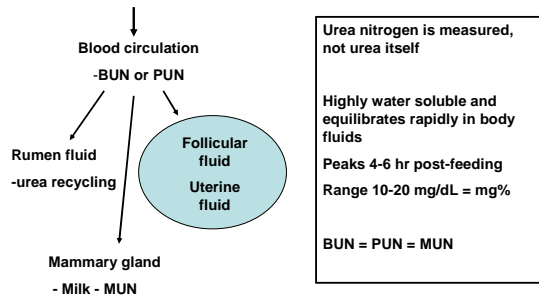
## Sources of urea in blood

- **Ruminal fermentation-RDP:** produces ammonia for incorporation into microbial protein, but some escapes and diffuses into portal blood for detoxification by the liver to urea.
  - The quantity of rumen ammonia produced and the amount that escapes for conversion to urea directly reflects both dietary RDP and the availability of fermentable CHO to support microbial growth and protein synthesis.

## Sources of urea in blood

- Second source of liver urea production is from deamination and metabolism of amino acids.
  - Circulating AA originate from intestinal absorption of RUP or microbial protein and mobilization of body protein.
  - AA not utilized for milk protein synthesis or deposition in tissue are deaminated by the liver to yield energy substrates and urea.

## Urea from liver



## MUN data- PA; Griswold et al., 2006

Table 4.

Effects of feeding method and daily average milk production on herd mean milk urea nitrogen (MUN) concentrations determined using DHIA individual cow records from Pennsylvania dairy herds (n = 196) during October 2005. Values are presented as mg/dL.

Variable	Least squares means	Standard error	Significance level
Feeding Method			0.0976
TMR-fed	15.25	0.81	
Component-fed	14.23	0.86	
Daily average milk production*			0.3661
< 60 lbs	14.20	0.79	
≥ 60 to < 67 lbs	14.45	0.85	
≥ 67 to < 75 lbs	14.80	0.84	
≥ 75 lbs	15.31	1.04	
Interaction of feeding method X daily average milk production			0.7114
TMR-fed			
< 60 lbs	14.78	0.94	
≥ 60 to < 67 lbs	15.30	0.92	
≥ 67 to < 75 lbs	15.49	0.91	
≥ 75 lbs	15.43	0.94	
Component-fed			
< 60 lbs	13.62	0.83	
≥ 60 to < 67 lbs	13.60	1.05	
≥ 67 to < 75 lbs	14.11	0.89	
≥ 75 lbs	15.50	1.54	

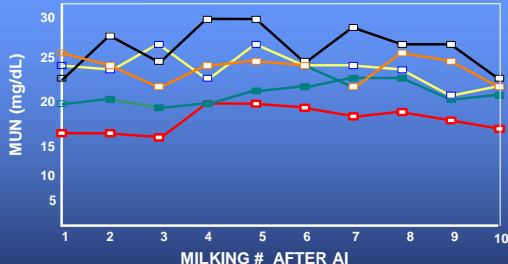
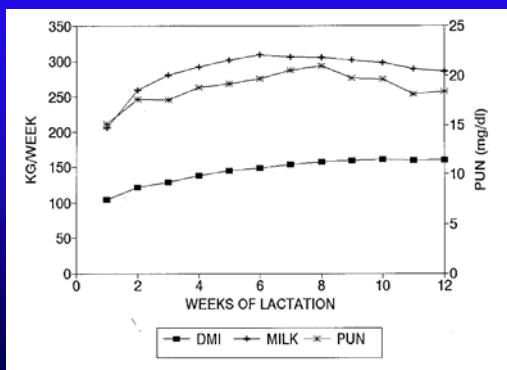
Herds feeding baylage had a greater MUN level than herds not feeding baylage (16.11 vs 15.22)

\*Based on quartile distribution of herd average daily production

## Blood urea concentrations in lactating cows

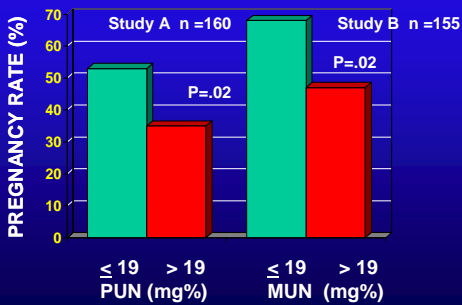
- Although the production of ammonia and urea can be minimized by balancing RDP and RUP, high dietary intake to support milk production and variation in rumen microbial yield make accurate prediction of the availability and balance of individual AA very difficult.
  - Consequently, most high producing cows consume protein in excess of requirements and blood urea concentrations are increased.

## PUN during early lactation



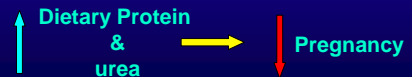
MUN provides a rapid, non-invasive and less expensive monitor of overall protein metabolism

## Pregnancy Rate vs. PUN or MUN



## High protein diets and urea (plasma or milk) are associated with decreased reproductive performance

- Westwood et al., (NZVetJ 46:123, 1998): Meta-analysis of 13 previous studies showed strong relationship for increased risk of conception failure with increased dietary protein content.
- Laven and Drew (VetRec 145:687,1999): Reviewed 15 studies on high protein diets and reported negative effects on fertility in most but not all.
- Wittwer et al., (PreventVetMed 38:159,1999): Increased MUN (>7.3 mmol/l) during spring in grazing herds (2153 cows in Chile) were associated with lower conception rates.
- Rajala-Schultz et al., (JDS 84:482,2001): High MUN (>15.4 mg/dl) was associated with lower risk of pregnancy (1728 cows).



## DHI MUN and conception rate to AI

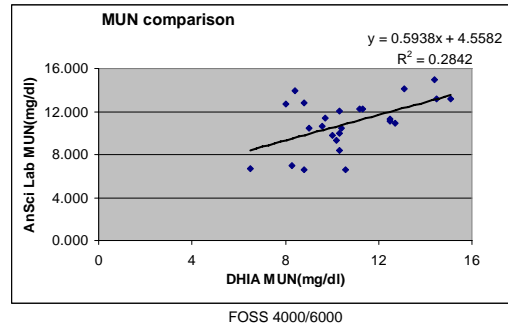
### Results are inconsistent

- Rajala-Schultz et al., (JDS 84:482,2001): High MUN (>15.4 mg/dl) was associated with 2.3X lower risk of pregnancy compared to <11.1 mg/dl (24 herds; 1728 cows).
- Godden et al., (JDS 84:1397,2001): limited utility for monitoring reproductive performance (60 herds).
- Guo et al., (JDS 87:1878,2004): MUN did not appear to affect CR% (713 herds; >10,000 cows).

### MUN instruments yield variable results

- Comparison of MUN analysis among 12 DHI laboratories in USA. Different instruments gave different values for the same milk samples. FOSS 4000 system was most variable and less consistent with other instruments. Kohn et al., (JDS 87:1848,2004); Peterson et al., (JDS 87:1747,2004).

**Causes confusion for interpretation of MUN measurements between herds and studies.**



## Conception and pregnancy result from an ordered progression of interrelated processes within the reproductive tract

- Ovarian follicular development and ovulation.
- Oocyte quality and fertilization.
- Embryo transport and development.
- Maternal recognition of pregnancy.
- Implantation.

Some toxic effect related to protein metabolism may interfere at one or more steps to impair fertility.

## Protein metabolism and sites of toxic effects for decreased fertility

- Ovarian follicular development and oocyte quality.
- Embryo transport and development.
  - Oviduct: 3-4 days
  - Uterus

## Dietary protein and associated changes in ovarian follicular fluid

Compared cows on day of estrus:

PUN (mg/dl)	ffl-UN (mg/dl)	ffl-Am ( $\mu$ mol/l)
Low 16-20	17	94
High 20-25	22*	308*

Hammon et al., An Reprod Sci (86:195, 2005)

Compared heifers on two diets:

PUN (mg/dl)	ffl-Am ( $\mu$ mol/l)	Oocytes cleavage (%)
16	205	62
20	267*	47*

Sinclair et al., JAS 2670, 2000



Oocyte health

## Dietary protein, PUN and associated changes in uterine fluid

Compared cows on day 7 after estrus:

PUN (mg/dl)	Utf-UN (mg/dl)	Utf-Am ( $\mu$ mol/l)
Low 16-20	21	1082
High 20-25	26*	1562*

Hammon et al., AnRepSci (86:195, 2005)

Embryo health & development



## Urea alters uterine environment

- Ions (Mg, K, P) Jordan et al., JDS 66:1845, 1983.
- pH
- Urea may interfere with normal inductive effects of progesterone on the microenvironment of the uterus, thereby causing suboptimal conditions for the support of early embryo development.

## Effects of urea and pH on embryo development *in vitro*

- Culture of early bovine embryos at pH 7 or lower (Uterine pH *in vivo* under high urea = 6.9) reduced development to blastocysts. (Ocon and Hansen, 2003)
- Culture of bovine embryos with urea at concentrations found in lactating cows reduced the proportion of oocytes becoming blastocysts and was attributed to decreased developmental competence of embryos formed from oocytes exposed to urea.

(Ocon and Hansen, JDS 86:1194, 2003; De Wit et al., JDS 84:1800, 2001)

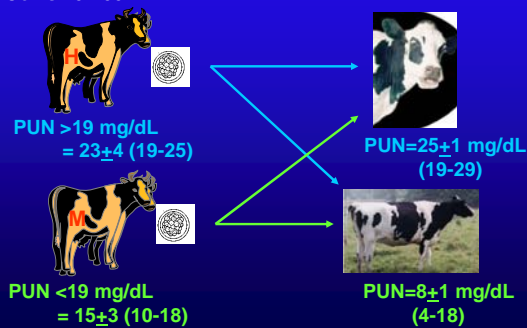
## Objective: To evaluate the effects of high PUN on quality and survivability of embryos from lactating cows

- Cows (40-100 DIM) fed isoenergetic diets to achieve moderate or high PUN (>19 mg/dL) for >30 days.
- Superovulation and embryo flushing (d7).
- Embryos evaluated and frozen.
- Embryos transferred to virgin heifers fed isoenergetic diets for low and high PUN levels for >30 days.
- Pregnancy diagnosis 28-40 days after ET.

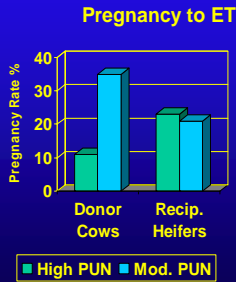
## PUN and Embryo Viability

Cows 40-100 DIM

Virgin Heifers



## Embryo Transfer Results



- High PUN in cows decreases embryo survival.
- PUN level in non-lactating recipients does not affect embryo survival after transfer.
- PUN affects oocyte/embryo viability before day 7 after AI.
- These results compared to no effect of high PUN on embryos of nonlactating cattle suggest an underlying impact of NEBAL on embryo survival that is exacerbated by high PUN.

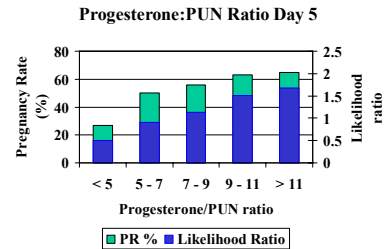
## Summary and Conclusions

- PUN >19 mg/dL is associated with decreased fertility in lactating dairy cows.
- High PUN alters the uterine environment and may affect embryo development.
- High PUN decreases embryo survivability and the effect occurs by day 7 after AI.
- The consequences of urea effects on the uterus may be to alter the rate of embryo development leading to asynchronous embryo/uterine interaction and early embryo loss.

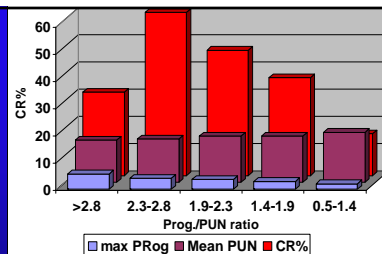
## Metabolic demands of high milk production are linked to protein metabolism and low fertility



**Higher progesterone reflects better metabolic status for pregnancy**



## Progesterone :PUN ratio after AI and fertility in lactating cows



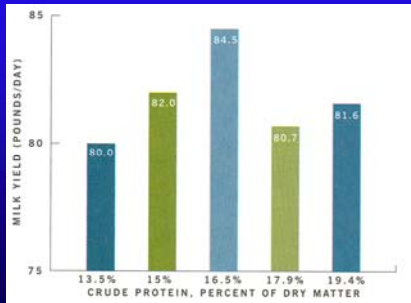
Prog:PUN	N	Prog <sub>max</sub> to d9 avg. (ng/ml)	PUN avg.	CR%	Likelihood of pregnancy
>2.8	26	5.6	15.6	31	0.74
2.3-2.8	25	4.0	16.0	60	2.50
1.9-2.3	26	3.4	17.1	46	1.43
1.4-1.9	25	2.8	17.1	36	0.94
0.5-1.4	26	2.0	18.4	15	0.3

## What nutritional strategies are available to minimize metabolic effects associated with poor reproductive performance??

- **Higher prepartum dietary protein (14-16% CP)**– seems most effective in maintaining or increasing prepartum DMI (VandeHaar et al., JDS 82:1282, 1999; Phillips et al., JDS 86:3634, 2003).
- During lactation, feed diets carefully **balanced with protein fractions** (RDP and RUP) at optimum ratios relative to requirements– this maximizes protein utilization for milk protein synthesis and **minimizes the negative impact of urea**.
- Products of protein metabolism (**urea & ammonia**) have been shown to **exert direct effects on oocytes, the uterine environment and early embryo development** in the uterus.
- **Urea is one of many factors to be considered in problem herds with low fertility, but negative energy balance is the most important problem.**

### CRUDE PROTEIN AFFECTS MILK YIELD

These cows achieved peak milk production at 16.5 percent crude protein. Going beyond that level did not result in extra milk production. In fact, it actually declined.



Schoonmaker, K. Dairy Herd Mgmt. August 2006, 37-40.

### Conclusions:

Poor fertility in high producing dairy cows reflects combined effects on oocyte competence and a progesterone dependent uterine environment that are rendered sub-optimum by earlier effects of negative energy balance and that can be further compromised by effects of urea resulting from intake of high dietary protein.

### Questions???

