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Milk Urea Nitrogen Concentration: Heritability and Genetic Correlations with Reproductive Performance and Disease in Holstein Cattle

Rissa G. Mitchell
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To the Graduate Council:

I am submitting herewith a thesis written by Rissa G. Mitchell entitled "Milk Urea Nitrogen Concentration: Heritability and Genetic Correlations with Reproductive Performance and Disease in Holstein Cattle." I have examined the final electronic copy of this thesis for form and content and recommend that it be accepted in partial fulfillment of the requirements for the degree of Master of Science, with a major in Animal Science.

Gary W. Rodgers, Major Professor

We have read this thesis and recommend its acceptance:

Gina M. Pighetti, Arnold M. Saxton

Accepted for the Council:
Dixie L. Thompson

Vice Provost and Dean of the Graduate School

(Original signatures are on file with official student records.)

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Anne Mayhew

Vice Chancellor and
Dean of Graduate Studies

(Original signatures are on file with official student records.)

MILK UREA NITROGEN CONCENTRATION: HERITABILITY AND GENETIC CORRELATIONS WITH REPRODUCTIVE PERFORMANCE AND DISEASE IN HOLSTEIN CATTLE

A Thesis

Presented for the

Master of Science

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Rissa G. Mitchell

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ABSTRACT

The objectives of this study were to estimate the heritability of milk urea nitrogen concentration (MUN), describe the genetic and phenotypic relationships between MUN and reproductive performance, and estimate correlations among MUN breeding values and Danish breeding values for disease in Holsteins. Dairy Records Management Systems in Raleigh, NC provided lactation data. The Danish Agricultural Advisory Center provided breeding value estimates for disease. Heritabilities, genetic correlations and phenotypic correlations were estimated with an animal model using ASREML. Infrared (IR) and wet chemistry (WC) data were analyzed separately. Heritabilities were estimated with all lactations, as well as separately for parities one and two. Genetic and phenotypic correlations were estimated separately for parities one and two. Herd-test-day effects, age at calving, and days in milk were included in all models. Heritability estimates for WC MUN were 0.15 for all lactations, 0.14 for first lactation, and 0.09 for second lactation. Heritability estimates for IR MUN were 0.22 for all lactations, 0.22 for first lactation, and 0.23 for second lactation. Genetic correlations between first and second lactation MUN values were greater than 0.97 for both WC and IR. Genetic correlations for WC MUN and various measures of reproductive performance, including days to first service (DFS), first service conception (FSC), services per conception (SPC), and interval from first service to conception (IFC), were generally found to be not different from zero. The genetic correlation between WC MUN and days open (DO) in first lactation was 0.21, and between WC MUN and DO in second lactation, was 0.41, indicating higher WC MUN values were associated with increased days open.

Phenotypic correlations were near zero for all measures. Genetic and phenotypic correlations for IR MUN and reproductive performance measures were not reported due to limited number of observations. Correlations among MUN breeding value estimates and Danish disease breeding values identified no significant relationships. Further investigations to identify possible non-linear relationships between MUN breeding values and Danish disease breeding values revealed no significant trends. While the results of this study indicate that heritable variation for MUN exists, the inability to identify significant genetic relationships to metabolic disease, reproductive performance, or foot and leg disease appear to greatly limit its use in selection for dairy cattle improvement in these areas at the present time.

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DFS	Days to first service
DHIA	Dairy Herd Improvement Association
DO	Days open
DPR	Daughter pregnancy rate
FLD	Feet and leg disease
FSC	First service conception rate
HTI	Health traits index
IFC	Interval from first service to conception
IR	Infrared analysis for milk urea nitrogen concentration
MDD	Metabolic and digestive disease
MUN	Milk urea nitrogen
NRC	National Research Council
PL	Productive life
RPD	Reproductive disease
SD	Standard deviation
SPC	Services per conception
WC	Wet chemistry analysis for milk urea nitrogen concentration

Chapter 1

Literature Review

SELECTION

Selection is the process through which improvement from one generation to the next is accomplished (14). The change in population mean produced by selection is often referred to as the response to selection. Response is a function of the heritability for a given trait, the selection intensity applied to that trait, and the phenotypic standard deviation (14). Heritability can be defined as the proportion of total variance for a given trait explained by genetics (6). Therefore, traits with high heritability estimates can be expected to yield a greater response to selection than lowly heritable traits (14). In dairy cattle breeding, traits with relatively high heritability estimates include body size, milk yield, fat yield, and protein yield (28,59).

Because milk sales are the primary source of income for most dairy producers and thus impact profitability so dramatically, selection programs in the US have placed a major emphasis on improving yield traits (23). Dairy cattle breeders have made considerable phenotypic and genetic gains through selection for yield traits over the past forty years. The average milk yield per year increased from 14,598 pounds per cow in the 1960's to over 23,000 pounds per year in the 1990's (59). Average breeding values for both cows and bulls also increased dramatically over this same time span (59).

While efforts to improve yield through selection have been extremely successful, they have not been without consequence. Detrimental correlated responses to selection for yield have been observed in the areas of reproductive performance and cow health by numerous researchers (24, 31, 50, 53, 55, 58, 62). In 1978, Shanks et al. (53) reported that daughters of high PTA milk sires had significantly higher costs for health care than did daughters of sires with average PTA milk. Hansen et al. (25), in a 1979 study, also documented increased health care costs for daughters of sires selected for high PTA milk versus daughters of sires that were breed average for PTA milk. In each case, the value of added milk yield offset the additional health care costs. Discussions with many of today's dairy producers indicate concern that this benefit to cost ratio is shrinking rapidly. Tight profit margins in the current dairy industry have resulted in increased interest to identify selection strategies that improve cow health and reproductive performance. Inclusion of health and reproductive traits in current selection schemes will likely only slow the rate of decline, or simply maintain present genetic levels of these traits. Increasing the emphasis on health and reproductive traits in selection goals would result in reduced selection pressure on yield traits, which may or may not be economically justifiable. Development of strategies that illustrate the possibility of continued selection for increased milk production without deleterious effects on fertility or cow health may be the most optimal solution (4).

Various researchers have documented evidence of considerable genetic variation in fertility measures and health disorders. The genetic standard deviation for days open was estimated to be six days by Hayes et al. (26). Berry et al. (4) and Veerkamp et al. (65) reported the genetic standard deviation of first service conception rate to be near

0.05%. Genetic standard deviation estimates of 7 days (46) and 9 days (65) have also been documented. Ketosis, milk fever, retained placenta, dystocia, lameness, and displaced abomasums have all been shown to have heritable genetic components (38, 55, 57, 62). Genetic variation found in reproductive and health traits indicates there is potential to respond to genetic selection.

Heritability estimates associated with health and reproductive traits are quite low. Denmark routinely collects data for all health and reproductive measures and publishes national genetic evaluations for such traits. Recently published heritability estimates for all health and reproductive traits are 0.05 or less (11).

Current efforts to include health and fertility in selection programs are focused on the publication of genetic evaluations for productive life and daughter pregnancy rates in the US. Productive life (PL) refers to the length of time a cow remains in the herd, from first calving to culling. Genetic selection for increased productive life is expected to result in improved production, fertility, and cow health (67). Heritability for productive life is estimated at 8.5% (59), however accurate estimates of breeding values are not available until late in a cow or bull's life. This somewhat limits the usefulness of this trait for selection purposes. The recent publication of genetic evaluations for daughter pregnancy rate (DPR) marks the first attempt to provide genetic summary information for reproductive traits in the US. Daughter pregnancy rate is calculated from days open data generated through the Dairy Herd Improvement Association (DHIA) system (64). Daughter pregnancy rate carries a heritability estimate of 0.04, along with a very low reliability until hundreds of daughters are summarized (64). Again this limits the effectiveness of this trait in contributing to progress in reproduction and health.

Application of genetic marker technologies certainly has potential to contribute to improvement in the areas of health and reproduction, however the long-term usefulness of this technology and its applications in dairy cattle breeding cannot be ascertained at this time (49). Considering the low heritabilities associated with reproductive and disease traits, genetic progress in these areas will likely come through selection for traits that are genetically correlated. Given that more rapid genetic progress can sometimes be attained through selection for a more heritable trait that is positively correlated with the desired trait (14), genetic progress in fertility and cow health may be feasible if appropriate indicator traits can be found. This strategy has already been proven effective with mastitis resistance. Indirectly selecting for improved udder conformation has resulted in cows that are less likely to have clinical mastitis (41). Selection for somatic cell scores are also used to indirectly select for reduced clinical mastitis (41). The identification of appropriate indicator traits to improve cow health and reproductive performance is of utmost importance if genetic progress is to be attained in these areas.

MILK UREA NITROGEN

Urea is considered a normal portion of the nitrogen components in milk. Urea concentration in milk occurs as the end result of protein metabolism (40). The breakdown of protein, both in the rumen and in the small intestine, results in the production of ammonia. The conversion of ammonia to urea occurs primarily in the liver, but also in lesser amounts in the kidneys (15). This process of conversion prevents the animal from suffering ammonia toxicity, as ammonia is highly toxic (15). Urea,

however, can be present in quite high concentrations without any apparent complications. Urea readily diffuses throughout all parts of the body and can easily be detected in the blood, milk, and urine (40). Urine serves as the primary excretion route from the body.

Numerous environmental factors are known to cause variation in MUN concentration. Protein intake, energy intake, and water intake will influence MUN concentrations (15). Consumption of higher protein diets results in greater MUN concentration. Conversely, increasing energy intake tends to decrease MUN. Increased water intake tends to lower MUN concentrations (15). Milk urea nitrogen may also vary according to the amount of time from feeding to milking, due to dilution effects (15). Further, variation is known to occur depending upon the type of ration fed. Total mixed rations are associated with lower MUN concentrations as compared with offering feed ingredients separately (22). Average MUN concentrations can also be expected to increase when cows are on pasture (40). Higher MUN concentrations have also been shown to occur in samples taken after morning feeding versus samples taken following afternoon feedings (22).

Monitoring milk urea nitrogen concentrations have proven helpful in evaluating herd nutritional status (19, 27, 32, 33, 52). Researchers have shown that elevated MUN levels are indicative of excess protein feeding for the given level of production (7) and may also reflect the ratio of protein to energy contained in the ration (34). Godden et al. (19) demonstrated that herds with high MUN means were associated with higher feed costs per kilogram of fat and lower income over feed costs per cow per day. Jonker et al. (33) developed target MUN values for cows fed according to National Research Council (NRC) recommendations, then compared these target values to actual field data in

Pennsylvania and surmised that, on average, cows were being fed 8 to 16% more protein than recommended by NRC. In a further study, Jonker et al. (32) demonstrated that providing dairymen with monthly MUN analysis could result in changes in feeding practices economically beneficial to dairymen. Nelson (43) predicted dairymen could expect to recover up to ten times the cost of MUN analysis by adjusting ration protein levels, thereby reducing feed costs and improving overall efficiencies. As result of such research, many herd nutritional consultants encouraged dairymen to seek MUN testing for their herds to evaluate rations for adequate protein utilization and efficiency.

Recent concerns with the impact of nutrient loss to the environment by production agriculture have created additional interest in MUN monitoring as well. Milk urea nitrogen concentrations have been shown to be highly correlated with both urinary and blood urea concentrations (7, 34, 35, 36). Because the majority of nitrogen loss to the environment occurs through excretion of urine and feces, monitoring MUN allows for the prediction of urinary nitrogen loss (27, 34, 35). Kohn et al. (36) and Jonker et al. (34) developed mathematical models to predict urinary nitrogen excretion from MUN analysis. Jonker et al. (32) predicted a significant decrease in nitrogen waste to the environment when dairymen were provided with monthly MUN analysis and instructed in its application for dietary protein balance.

In response to producers demand, coupled with the development of infrared MUN analysis technology, many Dairy Herd Improvement Associations (DHIA) began to offer routine MUN analysis in conjunction with monthly milk, fat, protein, and somatic cell analysis to their participating producers. Prior to the early 1990's, the available means of analysis for MUN concentration was the wet chemistry method. Wet chemistry analysis

(WC) involves the addition of reagents known to react specifically with urea. The reaction results in a color change that is then analyzed with a spectrophotometer. Correlations based on the intensity of color change measured are used to calculate MUN concentration in the sample (15). Wet chemistry analysis had not been widely adopted due to the amount of time required and the expense of testing. In the early 1990's the adaptation of existing infrared (IR) technology allowed MUN analysis to be completed quickly and economically (19). The IR technology had already been used for some time in the accurate analysis of butterfat and protein content of milk. Analysis for MUN was completed simultaneously with fat and protein analysis, using the same sample and laboratory machine for all three analyses (42).

Concerns soon arose with IR MUN analysis due to the method by which MUN values are generated. The analysis involves passing a beam of infrared light through the sample of milk and analyzing the wavelengths of light that are reflected by the sample (21). The wavelength reflected by urea is also known to be reflected by numerous other components in milk, including butterfat, lactose, true protein, citrate, and somatic cells (21). Varying quantities of these interfering components in the sample analyzed can bias the estimate either positively or negatively (30). Measurements of the other components allows for adjustments to be made in the final estimate of urea concentration. Therefore, the analysis of MUN by IR methodology is an indirect estimate, rather than an exact measurement of MUN concentration (21). Due to the fact that cows will exhibit differences in the concentrations of these other interfering components, IR estimates are known to produce different MUN values for multiple samples that have the same true MUN concentration (21).

Various researchers evaluated the IR analysis for accuracy in MUN prediction. Work by Kohn et al. (36) documented higher individual sample standard deviations from IR analysis than WC. Their research also indicated a tendency of IR analysis to overestimate low MUN and underestimate high MUN concentrations on individual cow samples. Schepers and Meijer (52) documented substantial variability with IR MUN analysis on an individual cow basis, however recommended bulk tank results could be interpreted reliably. Broderick et al. (7) also reported large differences for individual cow results with IR MUN values and recommended a minimum of 16 cows per ration group should be analyzed for results to be meaningful for management decisions. Since early work to identify MUN's relationship to nutritional parameters was conducted using wet chemistry analysis and had been interpreted on an individual cow basis, Godden et al. (19) hypothesized that results from IR MUN analysis interpreted on a group basis may, in fact, differ from earlier recommendations. Their research validated the use of IR MUN results for monitoring nitrogen efficiency in commercial herd situations. All cited references indicate the need for interpretation of IR MUN analysis on a group or herd basis, rather than individual cow basis (7, 19, 36, 52).

In the fall of 1998, personnel at National DHIA identified hardware defects with the machine used to generate calibration samples for DHIA laboratories across the US (36). Rectification of this defect resulted in MUN values generated after September 1998 being approximately 4.0 mg/dl lower than previously estimated (36). Calibration methodology has been standardized for all DHIA laboratories processing samples for MUN since this date (36). Current calibration standards are generated using wet chemistry methodology, with analysis performed by six different labs and the average

results used as the true MUN (42). Examination of MUN quality control statistics compiled by National DHIA (42) reveal obvious advantages for wet chemistry analysis. DHIA labs utilizing wet chemistry machinery exhibited substantially higher correlations with true MUN values than labs using IR machinery (42). Wet chemistry is widely accepted in the industry as more accurate, and is recommended when individual sample accuracy is required. National DHIA only recommends use of infrared results when the entire herd is analyzed and group results are averaged to make herd nutrition decisions (42).

MILK UREA NITROGEN AND REPRODUCTIVE PERFORMANCE

Reproductive performance of dairy cows is known to greatly impact profitability for dairy producers (2). Several studies have indicated that feeding excess protein to dairy cows can have a negative impact on fertility (9, 13, 16). As result of excess protein feeding, higher concentrations of urea can be detected in bodily fluids, including blood and milk (37). Higher than normal urea concentrations have been implicated in reducing fertility by altering uterine pH, thus creating a less than favorable environment for embryo survival (13). Circulating urea in the female reproductive tract may also impact conception by reducing sperm viability (12).

The negative association between high MUN concentrations and fertility has been widely reported (8, 37, 39, 47, 60). Larson et al. (37) demonstrated cows with high MUN concentrations (>21 mg/dl) at breeding were more likely to return to estrus at 21 days following breeding, and were less likely to become pregnant as MUN values increased.

MUN concentrations of greater than 19mg/dl on the day of insemination were associated with a 20% lower pregnancy rate in work completed by Butler et al. (8). Rajala-Schultz et al. (47) observed that cows with mean MUN concentrations in excess of 15.4 mg/dl for the month preceding breeding were significantly less likely to be confirmed pregnant than cows with MUN values of less than 15.4 mg/dl. In a commercial herd in Florida, Melendez et al. (39) documented a higher risk of non-pregnancy for cows bred during the summer with MUN concentrations exceeding 16 mg/dl in the 30 days preceding first service compared to cows with lower MUN values bred in the winter months. Vallimont et al. (60) analyzed test day records for 22,000 cows with MUN recorded within 30 days of first service. Analysis was conducted separately for IR and WC methodologies. Results for both IR and WC data indicated cows with extremely low MUN values (<6 mg/dl) and high MUN values (>18 mg/dl) exhibited a reduced likelihood of conception. Cows with intermediate MUN values of 6 to 9 mg/dl had the highest likelihood of conception.

MILK UREA NITROGEN AND COW HEALTH

Health issues, including metabolic disease and lameness, have become increasingly problematic, as herd production levels have risen over the past few decades. Common metabolic disorders of dairy cattle include ketosis, milk fever, and displaced abomasums. Ketosis usually occurs in the early weeks of lactation. Rapid utilization of body reserves and impaired carbohydrate metabolism are involved in the development of ketosis (63). Ketosis is more frequent when cows are over conditioned at calving and

postpartum rations are high in energy and low in roughage (3). Low blood sugar levels are the most prevalent indicator of ketosis (63). Milk fever also typically occurs very early in lactation, usually within 3 to 4 days after calving (3). Initiation of lactation results in a sudden mobilization of calcium due to the amount of calcium secreted in milk. Low blood calcium is the most significant characteristic of milk fever (3). Cows that received calcium dense diets in the dry period are much more prone to develop milk fever (63). Potassium rich diets have also been demonstrated to significantly increase the incidence of milk fever (29). Displaced abomasums occur when the abomasal compartment of the stomach twists resulting in blockage (63). Eighty to ninety percent of displaced abomasums occur during the first month of lactation. Cows with excess body condition at calving are at increased risk of displaced abomasums (54). Transition cows provided diets low in roughage content are also more likely to develop displaced abomasums (54). All these metabolic diseases are known to be influenced by nutritional parameters, but also have heritable components (49), however heritability estimate for metabolic disease are very low (11).

Foot and leg diseases, including lameness, have been implicated in increasing culling levels, reducing milk yield, and compromising reproductive performance (5, 48). Days to first service, days open, and services per conception are all increased when lameness occurs (44). Lameness is correlated with metabolic disease (45). Cows that experience difficulty or discomfort walking may not be getting adequate feed intake, resulting in increased incidences of metabolic disorders. Feeding of high-energy diets that are relatively low in forage to concentrate ratio also are known to increase the incidence of laminitis (5).

Both metabolic diseases and foot and leg diseases are known to be affected by nutritional management. MUN analysis is an effective means to evaluate nutritional status in dairy herds. Perhaps inherent genetic differences in cows' abilities to metabolize protein could account for a portion of the differences observed in disease susceptibility. Development of breeding values for MUN could be useful in future selection programs aimed at minimizing disease.

CONCLUSIONS

Dairy cattle selection programs have been very successful in producing both phenotypic and genetic gains in milk yield over the past several years. However, these gains have not been without consequence. Declines in reproductive performance and cow health have been documented. Costs associated with reduced fertility and increased disease susceptibility significantly impact producer profitability in the dairy industry. Breeders and geneticists are diligently searching for effective methods of including these important traits in current selection programs.

Incorporating traits into selection programs successfully requires that traits are measurable and have heritabilities of such magnitude that selection will yield a favorable response. Published heritabilities for reproductive and health traits are quite low, especially from data collected in a less than ideal recording program. Additionally, in the US there is no system in place to insure complete and accurate recording for these traits. Genetic progress in reproductive performance and cow health will likely rely on the identification of indicator traits.

Milk urea nitrogen concentration is an easily measured trait in our dairy cattle population. Clearly research has established that a phenotypic relationship between MUN and fertility exists. Furthermore, nutrition has been documented to play a pivotal role in the occurrence of numerous metabolic and locomotive diseases. MUN concentration is currently used to evaluate the nutritional status of lactating cows. Potentially, MUN could be used as an effective indicator trait for reproductive performance and/or cow health in selection programs.

This study was designed to identify the proportion of variation in MUN concentrations that can be attributed to genetic differences and to explore the possibility of genetic relationships between MUN and various measures of reproductive performance and cow health.

Chapter 2

Milk Urea Nitrogen Concentration: Heritability and Genetic Correlations with Reproductive Performance and Disease in Dairy Cattle

ABSTRACT

The objectives of this study were to estimate the heritability of milk urea nitrogen concentration (MUN), describe the genetic and phenotypic relationships between MUN and reproductive performance, and estimate correlations among MUN breeding values and Danish breeding values for disease in Holsteins. Lactation data was provided by Dairy Records Management Systems in Raleigh, NC. The Danish Agricultural Advisory Center provided breeding value estimates for disease. Heritabilities, genetic correlations and phenotypic correlations were estimated with an animal model using ASREML. Infrared (IR) and wet chemistry (WC) data were analyzed separately. Heritabilities were estimated with all lactations, as well as separately for parities one and two. Genetic and phenotypic correlations were estimated separately for parities one and two. Herd-test-day effects, age at calving, and days in milk were included in all models. Heritability estimates for WC MUN were 0.15 for all lactations, 0.14 for first lactation, and 0.09 for second lactation. Heritability estimates for IR MUN were 0.22 for all lactations, 0.22 for first lactation, and 0.23 for second lactation. Genetic correlations between first and

second lactation MUN values were greater than 0.97 for both WC and IR. Genetic correlations for WC MUN and various measures of reproductive performance, including days to first service (DFS), first service conception (FSC), services per conception (SPC), and interval from first service to conception (IFC), were generally found to be not different from zero. The genetic correlation between WC MUN and days open (DO) in first lactation was estimated to be +0.21, and +0.41 in second lactation, indicating higher WC MUN values were associated with increased days open. Phenotypic correlations were near zero for all measures. Genetic and phenotypic correlations for IR MUN and reproductive performance measures were not reported due to limited number of observations. Correlations among MUN breeding value estimates and Danish disease breeding values identified no significant relationships. Further investigations to identify possible non-linear relationships between MUN breeding values and Danish disease breeding values revealed no significant trends. While the results of this study indicate that heritable variation for MUN exists, the inability to identify significant relationships to metabolic disease, reproductive performance, or foot and leg disease appear to greatly limit its use in selection for dairy cattle improvement in these areas at the present time.

INTRODUCTION

Traditional selection programs employed by dairy cattle breeders have been extremely successful in improving yield traits (59). The undesirable correlated response to this selection strategy has been a decline in overall cow health and reproductive

performance (24, 31, 50, 53, 55, 58, 62). This has resulted in increased efforts to develop selection criteria to improve cow health and reproductive performance.

While evidence exists for considerable genetic variation in fertility measures (4, 26, 46, 65) and disease resistance (38, 55, 57, 62), heritability estimates for these traits are generally low. Recently published genetic evaluations for daughter pregnancy rate, which is calculated from days open data, has a heritability estimate of 0.04 (64). At the present time, no uniform method for collection of health data exists in the US. Denmark employs a mandatory, centralized recording system for all health traits and publishes national genetic evaluations for numerous health and reproductive traits. Published heritability estimates for all health and reproductive traits are 0.05 or less (23).

Milk urea nitrogen (MUN) is considered to be a normal non-protein nitrogen component in milk. Urea concentration in milk results as a by-product of the protein metabolism (40). Digestion of dietary protein results in the production of ammonia. Ammonia is converted to urea primarily in the liver (15). Urea is then excreted from the body primarily through urine, but is also found in blood and milk (40). Monitoring MUN levels have been utilized to evaluate herd nutritional status, as well as assess nitrogen excretion to the environment (34).

Many dairy herd improvement programs routinely offer MUN analysis to participating herds. Elevated MUN concentrations have been documented to adversely affect fertility (8, 37, 39, 47, 60). Evidence of a phenotypic relationship between MUN concentrations and reproductive performance suggest the possibility that genetic evaluations for MUN could be useful in selections programs to improve reproductive performance and cow health.

The objectives of this study were threefold. Our first objective was to estimate the heritability of milk urea nitrogen concentration. The second objective was to describe the genetic and phenotypic relationships between MUN and reproductive performance. Finally, our third objective was to estimate correlations among MUN breeding values generated from US lactation records and Danish breeding values for disease.

MATERIALS AND METHODS

Data

Lactation records including milk urea nitrogen data obtained from Dairy Records Management Systems in Raleigh, North Carolina were utilized in this study. Milk urea nitrogen concentrations were measured by either infrared or wet chemistry methods on test day samples routinely collected through the Dairy Herd Improvement system.

The initial data set included 625,000 lactation records. Records were edited to include only Holstein cows with valid identification from herds with more than ten cows per test day and greater than 75% of the cows within the herd having valid MUN data for each test day. Further edits eliminated records with missing or illogical birth or calving dates, days in milk greater than 305, parities greater than 5, and MUN values greater than 40. A minimum of five contemporaries were required, with contemporaries for heritability analysis defined as cows of the same parity that had MUN recorded for the same herd test day. Cows entering a herd in mid-lactation and records with indications of abnormal samples were eliminated. Edits also eliminated records with test days prior to October 1998 to insure uniform calibration standards across all laboratories. First

lactation records were edited to include cows that calved after 20 months of age and prior to 36 months of age. Second lactation records were edited to include cows that calved after 30 months of age and prior to 60 months of age. Table 1 describes the initial data set before and after edits.[1]

Table 2 contains a summary of records used in heritability estimations. The final data set for heritability estimates for all lactations totaled 83,058 records for IR MUN and 174,259 records for WC MUN. First lactation records used for heritability estimates were 38,355 for IR MUN and 78,144 for WC MUN. Second lactation records used for heritability estimates were 25,519 for IR MUN and 55,476 for WC MUN.

The initial data set also included reproductive performance information. Prior to analysis to determine correlations between MUN and reproductive performance, edits were made to exclude records with indicated days to first service (DFS) less than 25 or greater than 200, days open (DO) less than 25 or greater than 365, and interval from first service to conception (IFC) less than 0 or greater than 340. The final data set for estimation of genetic and phenotypic correlations between MUN and various reproductive performance measures is described in Table 3.

Breeding values for metabolic and digestive disease (MDD), reproductive disease (RPD), and foot and leg disease (FLD) in first and second lactations in Denmark for 64 bulls that also had daughters with MUN were obtained from the Danish Agricultural Advisory Center (Aarhus, Denmark). Principles of Danish Cattle Breeding (11) outlines procedures utilized in the calculation of breeding values and identifies diseases included

[1] All tables are located in Appendix 1.

in each disease category. A detailed description of diseases included in each of the disease categories can be found in Table 4.

Breeding values and reliabilities for MUN (regardless of test method), WC (MUN data derived from wet chemistry evaluations), and IR (MUN data derived from infrared evaluations) were generated for sires with a minimum of ten daughters with MUN data through ASREML for both first and second lactations. Data were edited to include only sires with a minimum reliability for MUN breeding values of 65% and a minimum disease reliability of 33%. A total of 64 sires were included for first lactation MUN and IR. Sixty-three sires met minimum requirements for inclusion in first lactation WC analysis. The analysis of second lactation breeding values for MUN, IR, and WC included 59, 56, and 55 sires respectively.

Analyses

All analyses were conducted using ASREML (18). Single trait animal models were used to estimate heritability and repeatability for MUN for first lactation, second lactation, and all lactations. Two trait animal models were used to estimate genetic and phenotypic correlations among first and second lactation MUN values. Two trait models were also utilized to estimate correlations between MUN and various reproductive performance traits.

All models used for heritability analysis included a 3rd order polynomial for age at calving and a 4th order polynomial for days in milk and a fixed herd test day effect.

Random effects for animal, permanent environment, and error were also included in the models.

Two trait animal models used to estimate correlations between reproductive performance measures and MUN also included polynomial terms up to third order for age at calving and polynomial terms up to fourth order for days in milk and a fixed herd-year-season of calving effect. Season of calving effects were defined as April through September and October through March. Random effects for animal, permanent environment, and error were again included in the models.

Sire breeding values for MUN, WC, and IR were obtained from ASREML solution files generated during the calculation of heritability estimates for each trait. Resulting sire breeding values were merged with breeding values for disease from Denmark. Correlations were calculated among breeding values for MUN, WC, IR, and Danish disease breeding values using PROC CORR in SAS version 8.02 (51). Breeding values for MUN, WC, and IR were then adjusted for reliability and approximate genetic correlations calculated among U.S. MUN values and Danish disease values. PROC GLM in SAS was then utilized to explore non-linear relationships between MUN, WC, and IR breeding values and Danish breeding values for disease.

RESULTS AND DISCUSSION

Milk Urea Nitrogen

Mean MUN data are summarized in Figure 1[2]. Mean MUN values tended to increase from first to second lactation. Previous studies by The Pennsylvania Center for Animal Health and Productivity (10), Wood et al. (68) and Vallimont et al. (60), all documented increased MUN values in second lactation. It is plausible that additional nutritional demands for growth in first lactation result in higher utilization of protein, thus lowering MUN excretion during first lactation.

The overall mean of 13.83 mg/dl across all lab types and lactations was comparable to results reported previously by other researchers. Jonker et al. (34) reported a mean of 13.51 mg/dl. Broderick and Clayton (7) reported a mean of 14.8 mg/dl. The Pennsylvania Center for Animal Health and Productivity (10) reported an overall mean of 13.03 mg/dl based on more than 4 million records. Wood et al. (68) reported a mean of 12.61 mg/dl for a dataset that included approximately 36,000 infrared MUN records. Again, this compares very favorably with the overall IR mean of 12.92 mg/dl in this study.

Heritabilities, genetic, and phenotypic correlations within first and second lactations are reported separately for each data type in Tables 5 and 6. Table 7 lists heritability estimates for each data type across all lactations. Heritability estimates for infrared data ranged from 0.22, in first lactation and across all lactations, to 0.23 in second lactation. Wet chemistry data yielded heritability estimates of 0.14 in first

[2] Figure located in Appendix 2.

lactation, 0.09 in second lactation, and 0.15 across all lactations. Standard errors for heritability estimates ranged from 0.01 to 0.03. Genetic correlations between first and second lactation MUN values were 0.99 for IR MUN and 0.98 for WC MUN. Approximate standard errors for the genetic correlations were 0.01 for both IR MUN and WC MUN.

Wood et al. (68) reported heritability estimates for infrared MUN data of much greater magnitude, ranging from 0.44 in first lactation to 0.59 in second lactation. Numerous characteristics of the current data set may partially explain the lower heritability estimates achieved by this analysis. First, Wood et al. (68) used a data set comprised of entirely registered animals that totaled approximately 36,000 records. The current data set includes animals of both registered and non-registered identity and totaled over 280,000 records. Inclusion of non-registered animals would likely result in increased pedigree recording error. Further, Wood et al. (68) included only lactation records with a minimum of four MUN observations. All MUN observations that met critical edits regarding minimum herd size and percentage of herd tested were included in this analysis. Analysis was completed with the imposed minimum of four MUN observations per lactation. Resulting heritability estimates increased 2-3%, however repeatability was not changed. Additionally, the Wood et al. (68) data set includes observations collected prior to October 1998 when MUN calibrations were standardized. No observations prior to calibration standardization were included in this analysis. Finally, Wood et al. (68) published heritability estimates for milk, fat, and protein, in addition to MUN. Heritability estimates for production components appear to be moderately high for some yield traits, as well. In particular, the heritability estimates for

fat with those data were 0.59 and 0.50 in second and third lactations respectively. Standard errors published for most traits also appeared somewhat higher than expected.

Heritability estimates were clearly higher for infrared data than wet chemistry data with IR estimates ranging from 0.22 to 0.23 and WC estimates varying from 0.09 to 0.15. This difference was somewhat surprising with possible explanations remaining unclear at the present time. Genetic correlations between infrared MUN and wet chemistry MUN in first and second lactations are reported in Table 8. Approximate genetic correlation between IR MUN and WC MUN in first lactation was 0.38 and 0.23 in second lactation. Standard errors of the genetic correlations averaged 0.08 in both first and second lactations. Phenotypic correlations are estimated much lower at 0.07 for first lactation and 0.04 for second lactation. These estimates indicate the possibility that IR MUN and WC MUN are actually measuring different traits.

This difference may in part be explained by the laboratory procedures involved in the two methods. Infrared MUN involves measuring the amount of light reflected by the milk sample at a specific wavelength then predicting MUN concentrations based on this result. The same technology has long been employed to estimate fat and protein concentrations in milk. Complications associated with infrared MUN include the knowledge that numerous other milk components, including butterfat, protein, and somatic cells reflect light at the same wavelength as urea. Interference of these other milk components is known to affect MUN estimates both positively and negatively, depending on the particular component. Because the concentration of these other interfering components is known to vary widely from cow to cow, differing MUN estimates can result from separate samples even when the true urea concentration is the

same (21). Vallimont et al. (61) conducted preliminary analysis to determine if MUN values should be adjusted for fat percentage and concluded that such adjustment had very little effect on the standard deviation of MUN and was therefore not warranted.

Wet chemistry methodology involves addition of an enzyme to a milk sample, then spectrophotometrically measuring the resulting color change to predict urea concentration (15). This method of evaluation is not impacted by the presence of other milk components, and has routinely been accepted by the industry as a more accurate prediction of true MUN (42). Because of this advantage in accuracy, perhaps WC MUN is a better indicator of genetic differences in individual cow's abilities to metabolize protein than IR MUN values.

Milk Urea Nitrogen and Reproductive Performance

Mean reproductive data by data type for first and second lactations are summarized in Table 9. Due to limited observations with MUN and reproductive performance measures, infrared data results are not reported. For wet chemistry data, average days to first service (DFS) were 85.8 in first lactation and 85.9 in second lactation. Days open (DO) averaged 140.3 in first lactation and 144.3 in second lactation. First service conception rates (FSC) averaged 27.3% in first lactation and 23.4% in second lactation. The mean interval from first service to conception (IFC) for first lactation was 53.6 days and second lactation mean was 57.3 days. The average services per conception (SPC) were 2.4 for both parities.

Heritability estimates for the various reproductive performance measures are listed in Table 10. Heritability estimates for days to first service were 0.04 in first lactation and 0.03 in second lactation. Days open had a heritability estimate of 0.05 for both parities. Standard error for first lactation was 0.03 and 0.04 for second lactation. Estimates of heritability for first service conception was 0.01 in first lactation and 0.00 in second lactation with standard errors of 0.01 and 0.02 respectfully. Interval from first service to conception heritability was estimated at 0.05 for first lactation and 0.00 in second lactation with standard errors of 0.03 for both estimates. First lactation heritability estimate for services per conception was 0.09 with a standard error of 0.04. Second lactation heritability estimate for interval from first service to conception and services per conception could not be estimated due to a failure to converge to a positive definite solution, which is characteristic of ASREML with small sample sizes and parameters near the boundary of the parameter space (17).

Genetic and phenotypic correlations between WC MUN and reproductive performance measures are documented in Table 11. With the exception of days open, genetic correlations between WC MUN and reproductive performance indicators were generally not different from zero, with estimates being less than or equal to the standard errors. Genetic correlations between WC MUN and days open were 0.21 in first lactation and 0.41 in second lactation. Approximate standard errors for genetic correlation were 0.17 in first lactation and 0.27 in second lactation. This indicates higher WC MUN concentrations can be associated with increased days open.

The phenotypic relationship between WC MUN and all measures of reproductive performance evaluated was near zero except for days open in second lactation. The

phenotypic correlation between WC MUN and days open in second lactation was estimated to be 0.04 with an approximate standard error of 0.02.

Milk Urea Nitrogen and Cow Health

Number of sires and mean breeding values by lactation and test method are listed in Table 12. A total of 64 sires had breeding values generated for MUN derived from first lactation records regardless of lab method with a mean of –0.17. Fifty-nine sires had breeding values generated for MUN in second lactation regardless of test method, also with an average of –0.17. Breeding values were estimated for sixty-four sires with records derived from infrared analysis from first lactation with a mean of –0.04. Fifty-six sires had breeding values calculated from infrared analysis during second lactation that averaged -0.02. Wet chemistry breeding values for first lactation were calculated for 63 sires and averaged -0.12. Breeding values for 55 sires were generated from second lactation wet chemistry analysis with a mean of -0.27. Tables 13 and 14 document breeding value correlations and approximate genetic correlations for U.S. generated MUN, IR, WC values and various Danish breeding values for disease within first and second lactations. No significant correlations were found, however all correlations between reproductive disease and MUN breeding values were negative for both parities and test methods, indicating a possible antagonistic relationship between MUN concentrations and reproductive performance. Correlations between MUN breeding values and metabolic disease and feet and leg diseases revealed no identifiable trends in either strength or direction of the relationship. Although no significant relationships were

identified, correlations between second lactation infrared breeding values and second lactation Danish breeding values for reproductive disease and feet and leg disease approached significance at $p<0.07$ and indicated a possible weak negative relationship of -0.25 for both categories.

Table 15 lists results of analysis conducted to identify relationships between U.S. MUN breeding values across all lactations and the Danish Health Traits Index (HTI). The Danish HTI is a standardized breeding value that indicates a bull's ability to sire daughters with increased resistance to diseases other than mastitis. The index includes reproductive, metabolic, and feet and leg diseases during the period of ten days prior to calving to 100 days post calving in first, second, and third lactations. No significant relationships could be identified. Additional analyses were conducted to explore possible non-linear relationships between US breeding values for MUN and Danish disease breeding values. Again, no significant trends were identified.

CONCLUSIONS

Heritability estimates from this study ranged from 0.09 to 0.15 for WC MUN and 0.22 to 0.23 for IR MUN. These estimates are significantly lower than previously reported estimates. Genetic and phenotypic correlations among MUN and various measures of reproductive performance were all generally found to be near zero, with the exception of wet chemistry MUN and days open. The genetic correlation between wet chemistry MUN and days open indicates higher WC MUN concentrations may be associated with increased days open. Correlations between US generated breeding values

for MUN and Danish disease breeding values revealed no significant relationships. Investigation of possible non-linear relationships between US MUN breeding values and Danish disease breeding values yielded no significant trends. While this study confirmed heritable variation for MUN exists, limited application of this information could be found for use in selection programs to improve cow health and reproductive performance.

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APPENDICES

APPENDIX 1. TABLES

Table 1. Composition of milk urea nitrogen (MUN) data set after edits.

Description	Observations
Initial records	625,000
All records with valid identification & MUN	280,104
All cows with valid identification & MUN	79,759
First lactation records with valid identification & MUN	123,247
First lactation cows with valid identification & MUN	42,147
Second lactation records with valid identification & MUN	87,362
Second lactation cows with valid identification & MUN	30,384

Table 2. Total observations for milk urea nitrogen (MUN) records, cows, and animals in first, second, and all lactations used in estimates of heritability by method of analysis.

	First Lactation		Second Lactation		All Lactations	
	IR[1]	WC	IR	WC	IR	WC
MUN records	38,355	78,144	25,519	55,476	83,058	174,259
Cows	13,950	25,902	9,544	18,671	26,540	46,951
Total animals in pedigree file	34,929	61,121	23,561	43,163	56,312	93,619

[1]IR=Infrared analysis, WC=Wet chemistry analysis.

Table 3. Total number of observations represented for reproductive data following edits for infrared (IR) and wet chemistry (WC) data in first and second lactations.

	IR		WC	
	First Lactation	Second Lactation	First Lactation	Second Lactation
MUN[1]	38,355	25,519	78,144	55,476
DFS	4,144	2,964	6,780	5,389
DO	2,495	1,529	4,356	3,161
FSC	1,237	734	1,848	1,263
IFC	1,219	779	2,463	1,866
SPC	2,570	1,574	4,490	3,239

[1]MUN=milk urea nitrogen, DFS=days to first service, DO=days open, FSC=first service conception rate, IFC=interval from first service to conception, SPC=services per conception.

Table 4. Description of diseases included in Danish Agricultural Advisory Center disease categories.

Danish Disease Category	Diseases Included
Feet and Leg Diseases (FLD)	Heel erosion Interdigital dermatitis Claw trimming by a veterinarian Interdigital necrobacillosis Interdigital skin hyperplasia Laminitis Arthritis Sole ulcer Pressure injury Tenosynovitis of hoof Other leg diseases
Metabolic and Digestive Diseases (MDD)	Diarrhea Traumatic reitculoperitonitis Ludigestion Hypermagnesemia Ketosis Milk fever Abomasal displacement Abomasal indigestion Rumen acidosis Enteritis Bloat Other digestive and metabolic diseases
Reproductive Diseases (RPD)	Abortion Endometritis Uterine prolapse Uterine torsion Endometritis treatment Follicular cysts Retained placenta Caesarian section Vaginitis Other reproductive diseases

Table 5. Heritabilities (h^2) and repeatabilities (rpt) on the diagonal (h^2/rpt), genetic (above diagonal), and phenotypic (below diagonal) correlations between infrared milk urea nitrogen (MUN) values in first and second lactations.[1]

	IR1[2]	IR2
IR1[2]	0.22/0.46	0.99
IR2	0.31	0.23/0.47

[1]Standard errors of heritabilities range from 0.02 to 0.03. Approximate standard error of genetic correlation was 0.01.

[2]IR1=Infrared MUN data from first lactation, IR2=Infrared MUN data from second lactation.

Table 6. Heritabilities (h^2) and repeatabilities (rpt) on the diagonal (h^2/rpt), genetic (above diagonal), and phenotypic (below diagonal) correlations between wet chemistry milk urea nitrogen (MUN) values in first and second lactations.[1]

	WC1[2]	WC2
WC1[2]	0.14/0.37	0.98
WC2	0.29	0.09/0.40

[1]Standard errors of heritabilities were 0.01. Approximate standard error of genetic correlation was 0.01.

[2]WC1=Wet Chemistry MUN data from first lactation, WC2=Wet Chemistry MUN data from second lactation.

Table 7. Heritability and repeatability estimates of infrared milk urea nitrogen (MUN) and wet chemistry MUN across all lactations.[1]

	Heritability	Repeatability
Infrared	0.22	0.40
Wet Chemistry	0.15	0.36

[1]Standard errors of heritabilities range from 0.01 to 0.02.

Table 8. Genetic and phenotypic correlations between infrared milk urea nitrogen (MUN) and wet chemistry MUN in first and second lactation.[1]

Lactation	Genetic Correlation	Phenotypic Correlation
First	0.38	0.07
Second	0.23	0.04

[1]Approximate standard errors of genetic correlations averaged 0.08 in both first and second lactation.

Table 9. Mean milk urea nitrogen concentration, days to first service, days open, first service conception rate, interval from first service to conception, and services per conception for cows measured by wet chemistry analysis among first and second lactations.

	Wet Chemistry	
	First Lactation	Second Lactation
MUN (mg/dl) [1]	13.91	14.70
DFS	85.8	85.9
DO	140.3	144.3
FSC (%)	27.3	23.4
IFC	53.6	57.3
SPC	2.4	2.4

[1]MUN=Milk urea nitrogen, DFS=Days to first service, DO=Days open, FSC=First service conception rate, IFC=Interval from first service to conception in days, SPC=Services per conception.

Table 10. Heritability estimates for days to first service (DFS), days open (DO), first service conception (FSC), interval from first service to conception (IFC), and services per conception (SPC) in first and second lactations.[1]

	First Lactation	Second Lactation
DFS	0.04	0.03
DO	0.05	0.05
FSC	0.01	0.00
IFC	0.05	0.00
SPC	0.09	…[2]

[1]The standard errors for heritabilities averaged 0.02 and did not exceed 0.04.

[2]Convergence to a positive definite solution failed.

Table 11. Genetic (Gen) and phenotypic (Phen) correlations between wet chemistry milk urea nitrogen concentrations and reproductive performance measures in first and second lactations.[1]

	First Lactation		Second Lactation	
	Gen (se)	Phen (se)	Gen (se)	Phen (se)
DFS[2]	-0.14 (0.15)	0.01 (0.01)	0.18 (0.21)	0.02 (0.02)
DO	0.21 (0.17)	0.01 (0.02)	0.41 (0.27)	0.04 (0.02)
FSC	-0.06 (0.24)	0.01 (0.01)	0.01 (0.52)	-0.03 (0.02)
IFC	0.11 (0.17)	0.00 (0.02)	…[3]	…[3]
SPC	0.17 (0.12)	0.00 (0.02)	…[3]	…[3]

[1]Approximate standard error for each estimate is shown inside parentheses adjacent to the corresponding estimate.

[2]DFS=days to first service, DO=days open, FSC=first service conception rate, IFC=interval from first service to conception, SPC=services per conception.

[3]Convergence to a positive definite solution failed.

Table 12. Number of sires, means, standard deviations (SD), minimums (Min), and maximums (Max) for milk urea nitrogen breeding values by test method and lactation.

	Sires	Mean	SD	Min	Max
MUN1[1]	64	-0.17	0.62	-1.69	1.97
MUN2	59	-0.17	0.64	-1.94	1.97
IR1	64	-0.04	0.89	-1.91	3.07
IR2	56	-0.02	0.95	-2.69	2.74
WC1	63	-0.12	0.56	-1.35	1.32
WC2	55	-0.27	0.55	-1.49	1.35

[1]MUN1=Breeding value derived from all first lactation MUN data regardless of test method, MUN2=Breeding value derived from all second lactation MUN data regardless of test method, IR1=Breeding value derived from all first lactation infrared MUN data, IR2= Breeding value derived from all second lactation infrared MUN data, WC1= Breeding value derived from all first lactation wet chemistry MUN data, WC2= Breeding value derived from all second lactation wet chemistry MUN data.

Table 13. Correlations and approximate genetic correlation estimates between breeding values for first lactation disease traits in Denmark and first lactation milk urea nitrogen (MUN) in the US.[1]

Disease Category	MUN[2]	IR	WC
	Breeding Value Correlations[3]		
Reproductive	-0.05	-0.04	-0.11
Metabolic and Digestive	0.03	-0.06	0.02
Feet and Leg	0.00	-0.11	0.02
	Approximate Genetic Correlations[4]		
Reproductive	-0.07	-0.06	-0.15
Metabolic and Digestive	0.04	-0.09	0.03
Feet and Leg	0.00	-0.17	0.03

[1]$p>0.39$ for all values

[2]MUN=Breeding value derived from all first lactation MUN data regardless of test method, IR=Breeding value derived from first lactation infrared MUN data, WC=Breeding value derived from first lactation wet chemistry data.

[3]Correlations between breeding values for disease in Denmark and US breeding values for first lactation MUN, IR, or WC

[4]Correlations between breeding values were adjusted for reliability of breeding values to approximate genetic correlations.

Table 14. Correlations and approximate genetic correlation estimates between breeding values for second lactation disease traits in Denmark and second lactation milk urea nitrogen (MUN) in the US.[1]

Disease Category	MUN	IR	WC
	Breeding Value Correlations[1]		
Reproductive	-0.24	-0.25	-0.12*
Metabolic and Digestive	0.05*	-0.06*	0.05*
Feet and Leg	-0.03*	-0.25	0.10*
	Approximate Genetic Correlations[2]		
Reproductive	-0.33	-0.35	-0.17*
Metabolic and Digestive	0.07*	-0.09*	0.08*
Feet and Leg	-0.04*	-0.38	0.16*

[1]p>0.06

[2]MUN=Breeding value derived from all second lactation MUN data regardless of test method, IR=Breeding value derived from second lactation infrared MUN data, WC=Breeding value derived from second lactation wet chemistry data.

[3]Correlations between breeding values for disease in Denmark and US breeding values for first lactation MUN, IR, or WC

[4]Correlations between breeding values were adjusted for reliability of breeding values to approximate genetic correlations.

*p>.39

Table 15. Correlations and approximate genetic correlation estimates between Danish health traits index (HTI) and breeding values for milk urea nitrogen (MUN) in the US.[1]

	Danish Health Traits Index	
	Breeding Value Correlation[3]	Approximate Genetic Correlation[4]
IR[2]	0.19	0.24
WC	-0.02	-0.03

[1]$p>0.13$

[2]IR=Breeding value derived from infrared MUN data across all lactations, WC=Breeding value derived from wet chemistry data across all lactations.

[3]Correlations between breeding values for disease in Denmark and US breeding values for first lactation MUN, IR, or WC

[4]Correlations between breeding values were adjusted for reliability of breeding values to approximate genetic correlations.

APPENDIX 2. FIGURES

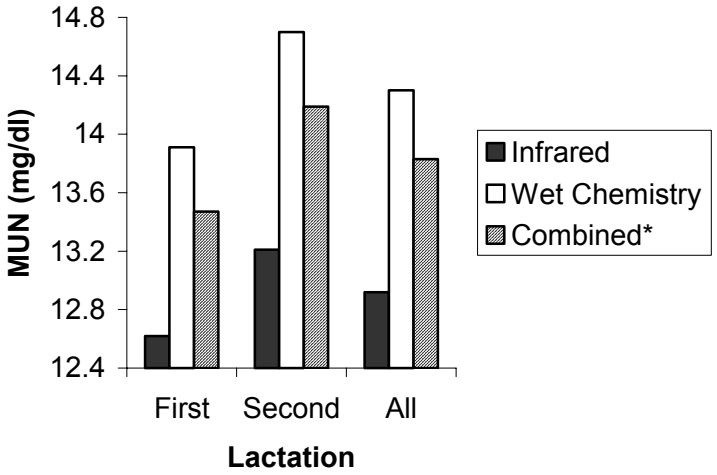

Figure 1. Mean milk urea nitrogen (MUN) values by analysis method at first, second, and all lactations.

*Includes MUN values derived from both infrared and wet chemistry analyses.

VITA

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