AN ABSTRACT OF THE THESIS OF

Noelle E. Muggli for the degree of Master of Science in

Animal Science presented on February 25, 1983

Title: INHERITANCE OF MATERNAL ANTIBODY CONCENTRATION IN THE BOVINE NEONATE

Abstract approved: Redacted for Privacy

William D. Hohenboken

Serum samples were collected between 24 and 48 h of age from 408 Hereford calves of a selection experiment and from 200 Angus, Hereford and Red Poll calves of another experimental population (Germ Plasm Utilization project). Concentrations of Immunoglobulin G_1 (IgG_1) were determined by single radial immunodiffusion. Breed or selection line of calf and age of dam were the most important factors influencing IgG_1 concentrations ($P < .01$). In the Germ Plasm Utilization (GPU) herd, Angus calves were highest, Red Polls were intermediate and Herefords were lowest in serum concentrations. Calves from Hereford lines selected for weaning weight, yearling weight or yearling weight and muscling score index were lower in IgG_1 concentration than calves from the randomly selected control line. In both populations immunoglobulin levels in the calf increased as age of dam increased. Calf sex did not affect IgG_1 in either population. In Selection Experiment Herefords, increased calving difficulty was associated with a

decrease in calf IgG_1 levels ($P < .05$). In the GPU population, as birth weight increased IgG_1 levels increased in the Angus, did not change in the Red Polls and decreased in the Herefords ($P < .05$).

Heritabilities of calf serum IgG_1 concentration, estimated from paternal half-sib analysis on a within line or breed basis, were .03 ± .09 and .13 ± .19 in the two populations. In the Selection Experiment Herefords, when the component of variance for selection line was added both to the numerator and denominator of h^2, the revised estimate was .09 ± .09. Heritabilities of maternal effects on IgG_1 concentration were also estimated (by nesting calves within maternal grandsires) on a within line or breed basis. These heritabilities were .23 ± .17 and -.07 ± .27 for the Selection Experiment and GPU populations, respectively. In the Selection Experiment population, when the variance component for selection line was added to the numerator and denominator of maternal effects heritability, the estimate was .27 ± .17. Those calves that died had a lower mean IgG_1 concentration than the overall population average ($P < .01$).

INHERITANCE OF MATERNAL ANTIBODY CONCENTRATION IN THE BOVINE NEONATE

by

Noelle Elizabeth Muggli

A THESIS

submitted to

Oregon State University

in partial fulfillment of
the requirements for the
degree of
MASTER OF SCIENCE

Commencement June 1983

APPROVED:

Redacted for Privacy

Professor of Animal Science in charge of major

Redacted for Privacy

Head of Department of Animal Science

Redacted for Privacy

Dean of Graduate School

Date thesis is presented February 25, 1983

Thesis typed by Noelle E. Muggli for Noelle E. Muggli

TABLE OF CONTENTS

LIST OF TABLES

INHERITANCE OF MATERNAL IMMUNOGLOBULIN G1 CONCENTRATION BY THE BOVINE NEONATE

INTRODUCTION

The calf is born with negligible levels of immune protection (Halliday et al., 1978), yet because the intestinal wall remains permeable to large protein molecules until approximately 24 h postpartum (Stott et al., 1979a), the calf can absorb immunoglobulins present in colostrum. If unable to receive this passive protection, the young animal is susceptible to many pathogens and death often results (McGuire et al., 1976). Previous results from this laboratory (Norman et al., 1981) suggested the existence of among and within breed genetic variation in the ability of newborn calves to acquire and absorb colostral antibodies.

Objectives of this experiment were to examine among and within selection line and breed variation in calf serum IgG_1 levels, to examine environmental sources of variation (sex of the calf, birth weight, gestation length, calving difficulty and age of the dam) on calf IgG_1 concentration, and to examine the relationship between IgG_1 concentration and growth traits and between IgG_1 concentration and survival potential of the calf.

MATERIALS AND METHODS

Populations and Management. Six hundred eight calves from two populations at the Roman L. Hruska U.S. Meat Animal Research Center (MARC) at Clay Center, Nebraska were involved in the experiment. During the 1982 spring calving season, 408 Hereford calves from four selection experiment lines and 200 calves (52 Red Poll, 90 Angus and 58 Hereford) from the Germ Plasm Utilization program were weighed at birth, and blood samples were taken between 24 and 48 h of age by venipuncture of the external jugular. After clotting had occurred, samples were centrifuged at 1,100 x g for 8 min and the serum was removed and stored at -20 C.

The Selection Experiment Hereford calves were from three 130-cow, 6-sire lines selected for weaning weight (WWL), yearling weight (YWL) and an index of yearling weight and muscling score (IXL). Calves from a randomly selected 215-cow, 10-sire control line (CNL) were also sampled. These lines were established in 1960 and have been maintained at MARC as one herd since 1971. A more detailed report of selection procedures and results was presented by Buchanan et al. (1982).

The Germ Plasm Utilization (GPU) animals were part of a larger project to evaluate heterosis retention and selection response in composite populations of beef cattle. Straightbred

Red Poll, Angus and Hereford herds, as well as other breeds, have been maintained as "controls" for that experiment.

The objectives of the experiment reported here were to evaluate genetic and environmental effects on the ability of the bovine neonate to acquire and absorb colostral IgG_1. Therefore, typical calving practices were altered only by acquisition of blood samples. If a calf was believed not to have suckled by 12 h of age, it was given assistance or manually fed by esophageal tubing a quantity of dam colostrum proportional to its body weight.

Laboratory and Statistical Analyses. The neonate serum samples were assayed for IgG_1 concentration by single radial immunodiffusion (SRID) gel procedures (Mancini et al., 1965). Antiserum to bovine IgG_1 was provided by Dr. Keith W. Kelley, Washington State University, Pullman, and was prepared as outlined by Kelley et al. (1982).

Plates were incubated for 48 h, and a calibrated RID viewer[1] was used for measurement of immunoprecipitate rings. Immunoglobulin standards[2] allowed estimation of sample IgG_1 concentration by logarithmic linear regression. In-house serum standards of known IgG_1 concentration were assayed on each

[1]Transidyne General Corp., Ann Arbor, MI 48106.

[2]Miles Research Product Division, Elkhart, IN 46514.

plate to determine intra- and inter-assay coefficients of variation, which were 7.03 and 10.12%, respectively. Each sample was assayed in duplicate, and the correlation between duplicate samples was .986.

To accomplish the objectives of this study, statistical analysis was done by least-squares analysis of variance (Harvey, 1975). Selection Experiment Hereford and GPU populations were analyzed separately. The mathematical models included breed or line of sire, sire or maternal grandsire within breed or line, age of dam, sex of calf and appropriate regression effects. All effects were assumed to be fixed except sire or maternal grandsire within breed or line and the residual. Heritability estimates of direct and maternal effects on IgG_1 concentration were computed from these analyses.

In a preliminary analysis, SRID assay run number and all biologically feasible two-factor interactions among the fixed effects were tested as potential sources of variation. These effects were not important. Comparisons among breeds, selection lines and dam age groups were made using Bonferroni t statistics (Gill, 1978). In additional analyses, linear, quadratic and cubic effects of birth weight and the interactions of these regressions with line or breed were included in the model. Birth date was also analyzed as a noninteracting covariate on IgG_1 concentration. Within the Selection Experiment Hereford population, the curvilinear effects of calving difficulty on

serum immunoglobulin concentration were analyzed on a within age group of dam basis. The effect of bleeding time, which ranged from 24 to 48 h of age, was also investigated in this population. The effect of gestation length on IgG_1 concentration was analyzed as a within breed regression in the GPU population.

IgG_1 levels and calf average daily gain through approximately 5 mo of age and through weaning were included as dependent variables in least-squares analyses of variance using the final model (breed or line, sire within breed or line, age of dam, sex and appropriate regression effects) in order to estimate genetic correlations between calf IgG_1 concentration and growth traits. Calves that were fostered were not included in these analyses.

RESULTS AND DISCUSSION

IgG_1 Levels. In Selection Experiment Herefords, the overall least-squares mean IgG_1 concentration was 25.5 mg/ml; and in the GPU calves, the least-squares mean was 34.7 mg/ml. The levels found in this study are consistent with levels reported in the literature of total Immunoglobulin G received passively, since IgG_1 comprises 65 to 75% of total IgG (Dawson and Cresswell, 1980). Klaus et al. (1969) reported 22.3 mg/ml of IgG in the sera of dairy calves at 24 h. McBeath and Logan

(1974) reported 30.9 mg/ml and 28.36 mg/ml of IgG for two consecutive years in suckled beef calves. Bradley et al. (1979) reported 25.7 mg/ml of IgG in calves of multiparous Herefords and 18.6 mg/ml in calves of primiparous Herefords. Levels of IgG_1 reported by Halliday et al. (1978) in suckler calves from Shorthorn X Galloway and Hereford X Friesian herds were 26.5 and 20.7 mg/ml, respectively. McGuire et al. (1976) reported a mean IgG_1 level of 37.5 mg/ml for beef calves that included Charolais, Hereford, Shorthorn and Angus at 2 to 7 d of age. Immunoglobulin concentrations decline after peaks seen between 24 and 48 h of age (Logan et al., 1974; McGuire et al., 1976; Halliday et al., 1978), so 24 h levels in their study probably were higher than their reported values. The higher levels reported by Norman et al. (1981), 48.2 and 47.2 mg/ml at 24 and 36 h of age, respectively, may be due to environmental and(or) management differences between experiments. In their study, each calf was assisted if it had not suckled by 3 h postpartum, insuring that the calf obtained colostrum during the most opportune time for immunoglobulin absorption. Also that study involved crossbred cows and calves, and breeds differed from those involved in this study.

Selection Experiment Herefords. Results of the analysis of variance are given in table 1. Selection line of calf was an important source of variation ($P < .01$). Calves from the randomly selected line (CNL) had the highest IgG_1 serum

concentrations (table 2). These results for selection and control line differences are supported by the findings of another study examining passive immunity. Bradley et al. (1979) reported that "control" Shorthorn calves had higher serum immunoglobulin levels of colostral origin ($P < .05$) than did calves of a line selected for 16 years on yearling weight criteria. If selection criteria (weaning weight, yearling weight and muscling score) have negative genetic correlations with Ig concentration, genetic improvement in those traits would lead to a decrease in immunoglobulin concentration. A negative correlation between birth weight and colostrum intake expressed as a percentage of birth weight (Selman et al., 1971a) indicates that smaller calves consume colostrum and subsequently colostral Igs in a higher proportion to their body weight than larger calves. A negative correlation between birth weight and serum IgG_1 concentration in lambs was reported by Cabello and Levieux (1981). These results suggest that the correlated response of increased birth weight to selection for increased growth rate (Koch et al., 1974) could have caused decreased immunoglobulin concentration in the weight selected lines. Yet in this population the within line effect of birth weight was not a significant factor in influencing levels of immunoglobulins. Also, the birth weight differences among selection lines were not consistent with differences among lines in Ig level. The differences between selected and nonselected lines may be due to factors more

intrinsic to the calf, such as differences in vigor at birth and therefore differential ability to acquire colostrum or in intestinal permeability causing differences in ability to absorb immunoglobulins. There may also be line differences in amount of colostral IgG_1 available to the calf.

The higher levels of IgG_1 in CNL calves might also be the result of a concentration factor. These lighter calves at birth ($P < .01$ in preliminary analysis) may have absorbed the same amounts of immunoglobulins yet, with a lower blood volume, the concentration of immunoglobulins in serum would be higher.

Age group of dam (table 2) had a highly significant effect on calf immunoglobulin concentration ($P < .01$). Calves of 2 yr old heifers had much lower serum levels than the overall mean for this population (19.9 mg/ml vs 25.5 mg/ml). Hafez (1964) suggested that the primiparous female may inhibit teat-seeking and so acquisition of colostral immunoglobulins by its newborn calf because of pain and shock experienced at parturition. The difference might also be due to inexperience at nursing and incomplete mammary development. The younger cow may not be producing the colostral quantity necessary to satiate pinocytotically-active epithelial cells in the intestine to allow maximum absorption by the calf. Other studies support this observation (Frerking and Aeikens, 1978; Bradley et al., 1979), reporting significant differences in calf serum immunoglobulins between primiparous and pluriparous dams. Calf IgG_1 levels

became higher as dam age group increased. Other studies have found a linear increase in calf maternal antibody concentrations as cow age increases (Frerking and Aeikens, 1978; Norman et al., 1981), and concentrations were higher in animals beyond three parities compared to younger animals (Mueller and Elleinger, 1981). However, correlations of neonate serum levels and maternal colostral concentrations are low (Klaus et al., 1969; McGuire et al., 1976; Hunter et al., 1977; Sawyer et al., 1977; Halliday et al., 1978; Norman et al., 1981). It may be that the volume of colostrum produced by the cow and consumed by the calf is more important in influencing the immunoglobulin level than the Ig concentration in the colostrum. Bush et al. (1971) reported that approximately 68% of the variation in calf blood serum Ig at 24 h was attributable to differences in Ig consumed per unit of weight. In 1973, Bush et al. reported that absolute amount of IgG consumed, not colostral IgG concentration, had a significant effect on blood IgG levels in the newborn calf. Stott et al. (1979b) reported that the age of the calf when fed colostrum and the amount fed were major factors in determining the Ig concentration in serum of the post-colostral calf. Increasing the amount of colostrum fed up to 2 liters resulted in increased serum concentrations. The older cows, then, may produce large amounts of high immunoglobulin concentration colostrum, and their calves could have the opportunity to receive

a saturating amount of immunoglobulins. Hence, the calf serum levels would be high.

Sex of the calf was not a significant source of variation in serum level of IgG_1, a finding in agreement with Bush et al. (1971), Sawyer et al. (1977), Bradley et al. (1979) and Norman et al. (1981).

Other researchers have reported that birth weight does not influence serum levels of passively-acquired immunoglobulins (Halliday et al., 1978; Bradley et al., 1979; Stott et al., 1979b; Norman et al., 1981). The results for this population support this conclusion, as the within line linear regressions of neonate serum concentration on birth weight were not significant.

In the study, age of dam and incidence of calving difficulty were closely related. The within age group regressions of IgG_1 levels on dystocia score were not significant but when pooled across cow age classes, dam dystocia affected calf IgG_1 level linearly ($P < .05$). Increased severity was associated with decreased concentration. Although dystocia may be stressful to the neonate and cause elevated cortisol levels soon after birth (Hudson et al., 1976), ACTH and associated adrenal steriods do not affect the permeability of the intestinal wall and hence immunoglobulin absorption (Cabello and Levieux, 1981; Rafai et al., 1981; Stott and Reinhard, 1978). Stott and Reinhard (1978) reported no difference in absorption of Immunoglobulins A, G and M in eutocial and dystocial calves fed equal amounts of pooled

colostrum. Hence, the effect of dystocia may be a maternally influenced factor. The 1970 study by Selman et al. indicates that a difficult calving may cause the cow to ignore or reject teat-seeking advances by the calf. Since time of suckling is crucial to immunoglobulin absorption, any delay could cause decreased levels in the calf.

Age at which the calf was bled influenced the concentration of immunoglobulin in the serum ($P < .05$). As age increased from 24 to 48 h, IgG_1 concentration decreased $.17 \pm .077$ mg/ml each hour. Serum levels of passively-acquired antibodies increase after colostrum feeding and reach a peak level believed to correspond to time of cessation of intestinal absorption. Concentrations decline thereafter, due to catabolism of the immunoglobulin proteins and to equilibration into extravascular tissue, until endogenous production of autologous antibodies begins (Klaus et al., 1969; Bush et al., 1971; Husband et al., 1972; Logan et al., 1972; Klobasa and Werhahn, 1981). Peak IgG_1 levels around 24 h were reported by Kruse (1970), Bush et al. (1971), Husband et al. (1972), Logan et al. (1974) and Stott et al. (1979a). The results of this study indicate that when bleeding commenced at 24 h, peak levels had been reached and degradation and(or) equilibration had begun. Cabello and Levieux (1981) suggested that timing of peak values is greatly affected by intestinal closure to macromolecules and that these values could be used as an index of duration of the intestinal

absorption period. Hence, pinocytotic activity had stopped by 24 h of age. During the following 24 h, there was a .17 ± .077 mg/ml decrease in serum IgG_1 each hour.

Birth date did not influence calf immunoglobulin level in the selection experiment population. This indicates that seasonal differences over the 6-wk calving period did not affect the calves' abilities to acquire and absorb maternal antibodies.

Germ Plasm Utilization Population. Breeds differed significantly in calf serum immunoglobulin concentration (table 3). Angus calves had the highest IgG_1 levels, Red Polls had intermediate levels and Herefords had the lowest concentrations (39.2 vs. 35.0 vs. 30.0 mg/ml, respectively). The breeds in this population experienced the same management and environmental conditions. Differences in calf vigor, maternal care, amount of colostrum available and colostral immunoglobulin concentration may have contributed to breed variation in the amount of immunoglobulins consumed. There might also have been differences among breeds in intestinal absorption.

Other studies, in both beef and dairy populations, have reported significant breed differences in calf concentration of maternal antibodies. Bradley et al. (1979) found highly significant differences among four beef breeds; Shorthorn calves had the highest levels, Simmental had the lowest and Hereford and Limousin calves were intermediate. Halliday et al. (1978) reported significantly higher levels of IgG_1 and IgM in colos-

trum and calf serum of Shorthorn X Galloway animals than in Hereford X Friesians. He also found significant breed differences in lambs' ability to concentrate colostral Igs, regardless of the ewe breed raising the lamb (1973). Significant beef breed effects were reported by Norman et al. (1981) for IgG_1 calf serum concentrations with Hereford- and Tarentaise-sired calves having higher levels than Simmental- and Pinzgauer-sired calves. Calves with Hereford X Angus sires were intermediate. In 1970, Kruse reported breed differences in increase of serum Ig concentration per kg of colostrum fed during the first 24 h after colostrum feeding and in absorption efficiencies between Jerseys, Black and White Danish (SDM) and Red Danish (RDM) calves. While Jersey animals absorbed more Igs than the SDM calves, they were less efficient in this ability. RDM neonates were poor in both factors. In a study by Selman et al. (1971b), Friesian X Ayrshire calves absorbed significantly greater quantities of immunoglobulin than similarily treated Ayrshire calves, and absorption was more efficient in the crossbred calves.

Age of dam again was a highly significant source of variation. The absence of 2-yr-old heifers in the GPU population sampled may account in part for the higher overall mean serum level of Herefords in this group than in the Selection Experiment Herefords (30.0 mg/ml vs 25.5 mg/ml, respectively). A linear increase in calf IgG_1 concentration was seen as age of dam increased until 7 yr when the mean level dropped (table 4). As

mothering ability and total immunoglobulin content of the colostrum increase with age, calf serum levels should increase proportionately (Bush et al., 1971; Selman et al., 1971a; Selman et al., 1971b; Frerking and Aeikens, 1978). The decreased levels in calves of 7 yr old cows seems unexplainable. However, production-related problems may have intervened and caused variation in calf IgG_1 levels. Logan and Gibson (1975) found the oldest cows in their study (> 8 pregnancies) to have a higher percentage of calves with low serum levels. They felt this was related to unsoundness of udders or to the presence of mastitis. Halliday et al. (1978) found some evidence that cows with mastitis transferred less immunoglobulins to their calves, possibly because of a reluctance of cows to allow suckling. The lower levels seen in calves of 7 yr old cows could be caused by a few cows having these conditions and negating the effect of high immunoglobulin concentration and colostrum production of other older cows.

While male calves tended to have higher Ig concentration than female calves in the GPU population, sex again was not a significant source of variation.

In the GPU population, the regression on birth weight within breed influenced passively-acquired immunoglobulin levels. The linear regression coefficients are presented in table 5. Angus calves showed an increase in IgG_1 concentration as birth weight increased ($P < .05$), Herefords decreased in concentration as

birth weight increased ($P < .05$), and levels of IgG_1 in the Red Polls were not affected by birth weight. Many studies have reported that birth weight does not affect levels of immunoglobulins absorbed into the blood (Halliday, 1974; Halliday et al., 1978; Stott et al., 1979b; Norman et al., 1981). However, Cabello and Levieux (1981) found a negative correlation between birth weight and colostral IgG_1 in the plasma of young lambs, while Kruse (1970) reported a significant positive correlation of birth weight and serum levels in Black and White Danish calves, but found no effect in the Red Danish breed.

The within breed of calf effect of gestation length on serum immunoglobulin concentration was investigated in the current experiment, and no significant regression was found. Cabello and Levieux (1981) found a negative relationship between length of gestation and lamb IgG_1 concentration ($r = -.8$). They suggested that shorter gestation length would be associated with less advanced physiological maturity, leading to longer absorption of Igs through the intestine. Since the duration of intestinal permeability of immunoglobulins has a major effect on the acquisition of passive immunity, the less mature lambs would have higher levels. In a 1974 study, Halliday reported that lamb concentration was significantly and positively correlated with gestation length. This was thought to be related to greater vigor at birth in those lambs with longer gestation, leading to enhanced ability to acquire immunoglobulins.

Calf birth date had no effect on the level of IgG_1 obtained from colostrum in this population.

Heritabilities and Genetic Correlations. Few studies have examined within-breed genetic variation in ability of ruminants to acquire passive immunity from colostrum. Halliday (1981) found low heritabilities in lambs and suggested that any improvement from selection for immunoglobulin transfer to the lamb would be slow. Norman et al. (1981) reported heritabilities of calf serum IgG_1 levels at 24 h of age to be .52 $\pm$ .28 and at 36 h to be .69 $\pm$ .30. Heritabilities of IgM levels were intermediate (.30 $\pm$ .26 and .35 $\pm$ .26 at 24 and 36 h, respectively).

In this study, heritability estimates for calf immunoglobulin levels were .03 $\pm$ .09 and .13 $\pm$ .19 for the Selection Experiment Hereford and the GPU populations, respectively (table 6). Thus, the moderate to high heritability estimates of Norman et al. (1981) were not substantiated by these results. However, genetic variability within the Selection Experiment Hereford base population was indicated since selection line was a significant source of variation on calf IgG_1 levels. To examine heritable differences in a reference population composed of the entire Selection Experiment Hereford population (as opposed to heritability within lines), the variance component for lines was added to both the numerator and denominator of the within line heritability estimate, and the parameter was recomputed. This heritability equalled .09 $\pm$ .09.

Age of dam and dystocia effects as reported previously indicated that calf IgG_1 level was strongly influenced by maternal factors. Since genetic variation may exist in concentration and amount of colostral immunoglobulins and in maternal behavior, which can influence time and amount of colostral intake, heritabilities were estimated for the maternal effect on calf IgG_1 concentration. These estimates, using the component of variance for maternal grandsires on a within selection line or breed basis, were .23 $\pm$ .17 and -.07 $\pm$ .27 for the Selection Experiment Hereford and GPU populations, respectively. In order to estimate the genetic variability in a Hereford reference population when considering calf IgG_1 level as a maternal trait, maternal grandsire and selection line variance components were used in the heritability estimation. This heritability was .27 $\pm$ .17.

Because the calf is born with negligible immunoglobulin levels, immune protection for the first months of life is dependent on passively-acquired immunoglobulins. The IgG_1 level could influence subsequent health, and health might be related to weight gains during that time period. In this study, the genetic correlations between IgG_1 concentration and two average daily gains, determined from birth to 5 mo of age and to weaning, were examined. In the Selection Experiment Herefords, the correlations were not estimable since negative sire variance components were found for both daily gains. In the GPU population, the correlation estimates were 1.60 $\pm$ 1.47 and 2.00 $\pm$ 2.40.

The population structure was therefore inadequate for accurate estimates. While Halliday et al. (1978) found a positive correlation between calf serum Immunoglobulins G_1, G_2, and M concentration and daily weight gain up to 42 d, the advantage in growth was transitory and had disappeared by 126 d of age.

Health and Survival. Several identifiable causes of interference of colostrum acquisition were observed in those calves with low IgG_1 serum levels (defined arbitrarily as those more than one standard deviation below the mean). Three of the six twin calves sampled were low. (Data on the twin calves were not included in previous analyses of variance.) This could be due to an inadequate amount of colostral immunoglobulins available to each twin. Thirty four and 11% of calves born to 2-yr-old and 3-yr-old cows, respectively, had low levels. These calves may have lacked proper maternal care. Twenty seven percent of the calves with low IgG_1 concentrations were born to cows that required assistance during parturition. The pain experienced during a difficult birth, or handling stress, may have caused poor maternal behavior towards these calves. Four older animals would not claim their young and required restraint and persuasion before they allowed suckling. Five calves could not obtain colostrum because of illness and one because of an accident. Age at first ingestion may have increased in these circumstances, and reduced absorption could have resulted. Thirty one percent of the calves with low levels had no identifiable cause for these

lower concentrations. The colostrum they received could have been of very low immunoglobulin content. Also, these calves may have received adequate amounts of colostrum, yet faulty mechanisms could have hindered immunoglobulin absorption.

Within the Angus herd, eight cows aggressively rejected advances by their calves. In most cases, the aggressiveness was so excessive that it was necessary to remove the calf until the cow's behavior could be controlled. Yet these calves had a mean IgG_1 level of 28.2 $\pm$ 4.09 mg/ml, a suprisingly high level under those conditions.

Selman et al. (1971b) and Stott et al. (1979c) demonstrated that actual suckling increased serum levels of Igs because of increased absorption efficiency. This was not due to increased consumption or younger age at suckling but rather a direct increase in pinocytotic activity and cellular transport by the intestinal epithelium, possibly caused by some labile substance present in the fresh colostrum (Stott et al., 1979c). Serum levels for the five animals fed dam colostrum through esophageal tubing were much lower (14.1 $\pm$ 1.31 mg/ml) than the overall mean serum level. While this may support the above finding, the difference could also be augmented by a delay in colostrum feeding time.

Although Sasaki et al. (1977) suggest that there is some antibody synthesis during the first days of life, onset of significant endogenous antibody synthesis occurs at a later age. A

range of estimates has been found; Husband et al. (1972) reported that production occurred at 8 to 16 d of age while Logan et al. (1974) reported that endogenous antibody synthesis began at 30 d. Husband et al. suggested that prior to appearance of these immunoglobulins, a decrease in exogenous antibodies because of biological degradation could cause a time of low levels and increased susceptability to invading pathogens. While hypogammaglobulinemic animals produce serum immunoglobulins at an earlier age than those animals with higher concentrations (Logan et al., 1974; Husband and Lascelles, 1975; McGuire et al., 1976; Klobasa and Werhahn, 1981), animals with initial low maternal levels may be extremely susceptible to infectious disease before this onset of antibody synthesis and until the time when protective levels have been reached (Husband et al., 1972).

Low levels of protecting immunoglobulins can increase the risk of death due to invading pathogens (McBeath and Logan, 1974; McGuire et al., 1976; Frerking and Aeikens, 1978; Myers, 1980). Results of this experiment lend support to this conclusion. Fourteen (3%) of the Selection Experiment Hereford calves died during the calving season, and one Angus calf died from enteritis at 20 d of age. These Herefords had a mean level of 16.1 $\pm$ 2.33 mg IgG_1/ml of serum, lower in antibody concentration than average for the entire population ($P < .01$). The Angus calf had an IgG_1 concentration of 16.7 mg/ml. Seven additional Selection Experiment calves died between the end of calving season and

weaning age. Their mean IgG_1 level was 23.7 $\pm$ 4.28. Thus, the increased risk of death because of low colostral immunoglobulin level was evident only during the first 50 d of life.

There is nonselective absorption of proteins by the highly vacuolated, immature epithelial cells of the neonatal intestine (Brandon and Lascelles, 1971; Sawyer et al., 1977). Halliday et al. (1978) reported that relative concentrations of IgG_1, IgG_2 and IgM in calf serum were almost identical to those in the colostrum and suggested that absorption by the calf was nonselective. While Husband et al. (1972) found greater apparent efficiency of absorption of the larger molecular weight IgM compared to IgG, he suggested that a higher proportion of IgG than IgM had left the bloodstream and entered the interstitial fluid. Hence, an underestimate of the quantity of IgG absorbed may have resulted. Klaus et al. (1969) found equal efficiency in absorption of IgM and IgG from the intestinal tract. Norman et al. (1981) reported a correlation of .66 between 24 h IgG_1 and IgM concentrations in calf serum. If the newborn serum levels are low in IgG_1, the calf may also be deficient in the other immunoglobulins and therefore deficient in pathogenic protection.

Hypogammaglobulinemia is not always fatal (Halliday, 1973, 1974). In the Selection Experiment Hereford herd, 67 calves or 16% were beyond one standard deviation below the mean of IgG_1 concentration, yet only five calves of this group died. There were 32 calves (16%) lower than one standard deviation below the

mean in the Germ Plasm Utilization population, and only one of them died. None of the dead calves was more then two standard deviations below the mean, while one and two live calves from the Selection Experiment and GPU populations, respectively, were found to be this low. Neonates with low amounts of maternally-acquired protection can remain healthy if exposure to pathogens is minimal (McGuire et al., 1976). Small amounts of antibodies against specific antigens in the young animal's system could provide the protection needed.

Immunoglobulin A is also an important component of passive protection and may provide local protection in the intestinal lumen of the young animal, as reviewed by Watson (1980). Because of its unique property of resisting proteolytic degradation within the stomach and intestine due to an additional protein component, IgA may provide protection even after cessation of intestinal absorption has occurred. It may be that animals with low IgG_1 serum concentrations had adequate amounts of IgA within the intestine to control invading pathogens.

Lack of appropriate specific antibodies could be the reason that some calves with apparently adequate immunoglobulin levels succombed to disease (McGuire et al., 1976). Four of the 12 calves that died during the calving season and seven of the 22 that died within the first 200 d of life were within 2 mg/ml of the mean Selection Experiment Hereford serum concentration, a level which would seem sufficient for protection.

There was no indication that calves with extremely high levels of maternal immunoglobulins were at an advantage because of greater immune protection. However, maternal antibodies can alter immunological responsiveness of the neonate, inhibiting the development of the humoral immune response. Husband and Lascelles (1975) reported an earlier increase in total immunoglobulins in colostrum-deprived calves than in those fed colostrum. Concentrations of IgG_1 and IgG_2 increased threefold between birth and eight days, while in colostrum-fed animals endogenous production did not occur until 8 to 16 d of age. Concentrations of all immunoglobulins were significantly higher in the deprived animals at 128 d of age ($P < .01$), indicating a feedback inhibition by the maternal immunoglobulins. They found a marked unresponsiveness to antigens injected at birth if colostral antibodies specific for the antigen used were present in the circulation. However, significant responses occurred against antigens to which there were no maternal antibodies. These responses were not as great as those in older calves similarly immunized; this suggests that age also influences the response.

CONCLUSIONS

This study failed to substantiate the high heritabilities for calf IgG_1 level found by Norman et al. (1981). However,

there was evidence of a moderate heritability when calf IgG_1 concentration was considered as a dam trait. Norman et al. (1981) found high repeatabilities of calf serum immunoglobulins at 24 and 36 hr of age when considered as traits of the cow (.47 + .11 and .45 + .16, respectively). Therefore, it may be possible to select for improvement in calf IgG_1 levels when selection pressure is placed on the dam rather than the calf.

Significant selection line differences were found. This suggests that a negative genetic correlation between calf IgG_1 concentration and growth traits (weaning weight, yearling weight and muscling score) might exist.

There was indication of a relationship between low IgG_1 level and decreased calf survival. However, not all calves with low levels died. Calves at risk of low concentration were born to young cows (2- and 3-yr-olds) and to cows that experienced a difficult parturition.

TABLE 1. LEAST-SQUARES ANALYSIS OF VARIANCE FOR SERUM IGG1 (MG/ML) IN SELECTION EXPERIMENT HEREFORD CALVES

Source of variation	df	Mean squares	F
Line	3	779.9	6.3 **
Calf sire/line	24	124.3[a]	1.1
Age group of dam[b]	2	3030.7	27.4 **
Sex	1	74.1	.7
Linear regression on calving difficulty	1	528.3	4.8 *
Residual	376	110.8	

[a]Error term for test of significance of line effects. The residual mean square was the error term for all other sources of variation.

[b]Age groups were 2-yr-old, 3-yr-old and 4-yr-old and older cows.

* $P < .05$
** $P < .01$

TABLE 2. LEAST-SQUARES MEANS AND STANDARD ERRORS FOR SERUM IGG1 (MG/ML) IN SELECTION EXPERIMENT HEREFORD CALVES

Effect	N	Mean	SE
Overall	408	25.5	.58
Line[a]			
WWL	91	25.3^{bc}	1.18
YWL	100	22.1^{b}	1.14
IXL	82	25.8^{bc}	1.24
CNL	135	28.6^{c}	1.00
Sex			
Female	196	25.9	.80
Male	212	25.0	.80
Age group of dam			
2 years	116	19.9^{b}	1.08
3 years	101	26.4^{c}	1.09
4-9 years	191	30.2^{d}	.84

[a]Line abbreviations are weaning weight (WWL), yearling weight (YWL), index of yearling weight and muscling score (IXL) and randomly selected (CNL).

[b,c,d]Means with different superscripts differ ($P < .05$).

TABLE 3. LEAST-SQUARES ANALYSIS OF VARIANCE FOR SERUM IGG1 (MG/ML) IN GERM PLASM UTILIZATION CALVES

Source of variation	df	Mean squares	F
Breed	2	1350.0	6.4 **
Calf sire/breed	22	211.4[a]	1.2
Age of dam	4	614.6	3.6 *
Sex	1	162.3	1.0
Linear regression on birth weight within breed	2	605.2	3.6 *
Residual	167	169.5	

[a]Error term for test of significance of breed effects. The residual mean square was the error term for all other sources of variation.

* $P < .05$
** $P < .01$

TABLE 4. LEAST-SQUARES MEANS AND STANDARD ERRORS FOR SERUM IGG1 (MG/ML) IN GERM PLASM UTILIZATION CALVES

Effect	N	Mean	SE
Overall	200	34.7	1.20
Breed			
Angus	90	39.2^{a}	1.72
Hereford	58	30.0^{b}	2.10
Red Poll	52	35.0^{ab}	2.39
Sex			
Female	94	33.7	1.59
Male	106	35.8	1.62
Age of dam			
3 years	70	31.8^{ab}	1.90
4 years	43	29.6^{a}	2.26
5 years	35	39.8^{b}	2.50
6 years	27	39.0^{ab}	2.79
7 years	25	33.5^{ab}	3.04

^{a,b}Means with different superscripts differ ($P < .05$).

TABLE 5. WITHIN BREED LINEAR REGRESSION OF SERUM IGG1 (MG/ML) ON BIRTH WEIGHT (KG)

Breed	Coefficient	SE
Pooled	.02	.059
Angus	.16 *	.080
Hereford	-.16 *	.100
Red Poll	.06	.106

* $P < .05$

TABLE 6. HERITABILITY ESTIMATES OF CALF SERUM IGG1 LEVELS

Population	h^2	SE
Selection Experiment Herefords, using calf sire variance component	.03	.09
Selection Experiment Herefords, using calf sire and selection line variance components	.09	.09
Selection Experiment Herefords, using maternal grandsire variance component	.23	.17
Selection Experiment Herefords, using maternal grandsire and selection line variance components	.27	.17
Germ Plasm Utilization herd, using calf sire variance component	.13	.19
Germ Plasm Utilization herd, using maternal grandsire variance component	-.07	.27

LITERATURE CITED

Bradley, J. A., L. Nilo and W. J. Dorward. 1979. Some observations on serum gammaglobulin concentrations in suckled beef calves. Can. Vet. J. 20:227.

Brandon, M. R. and A. K. Lascelles. 1971. Relative efficiency of absorption of IgG_1, IgG_2, IgA and IgM in the newborn calf. Australian J. Exp. Biol. Med. Sci. 49:629.

Buchanan, D. S., M. K. Nielson, R. M. Koch and L. V. Cundiff. 1982. Selection for growth and muscling score in beef cattle. I. Selection applied. J. Anim. Sci. 55:516.

Bush, L. J., M. A. Aguilera, G. D. Adams and E. W. Jones. 1971. Absorption of colostral immunoglobulins by newborn dairy calves. J. Dairy Sci. 54:1547.

Bush, L. J., M. B. Mungle, L. D. Corley and G. D. Adams. 1973. Factors affecting absorption of immunogobulins by newborn dairy calves. J. Dairy Sci. 56:312.

Cabello, G. and D. Levieux. 1981. Absorption of colostral IgG_1 by the newborn lamb: influence of the length of gestation, birth weight and thyroid function. Rec. Vet. Sci. 31:190.

Dawson, J. R. and P. Cresswell. 1980. Immunogens (antigens) and antibodies and their determination. In: W. K. Joklik, H. P. Willett and D. B. Amos (Ed.) Zinsser Microbiology. p 315. Appleton-Century-Crofts, New York.

Frerking, H. and T. Aeikens. 1978. About the importance of colostrum for the newborn calf. Ann. Rech. Vet. 9:361.

Gill, J. L. 1978. Nonorthogonal designed contrasts (Bonferroni t statistics). In: Design and Analysis of Experiments in Animal and Medical Sciences. pp 176-177. The Iowa State University Press, Ames.

Hafez, E. S. E. 1964. Some physiological and behavioural responses of the neonate. Cornell Vet. 59:545.

Halliday, R. 1973. Serum immunoglobulin concentrations at two days of age in lambs born after ova transfer between ewes of different breeds. J. Agr. Sci. (Camb.) 81:29.

Halliday, R. 1974. Variations in immunoglobulin concentrations in Merino and Scottish Blackface lambs. Anim Prod. 19:301.

Halliday, R. 1981. Antibody transfer from ewes to lambs. Anim. Breed. Res. Org. Annu. Rep., 1981.

Halliday, R., A. J. F. Russel, M. R. Williams and J. N. Peart. 1978. Effects of energy intake during late pregnancy and of genotype on immunoglobulin transfer to calves in suckler herds. Res. Vet. Sci. 24:26.

Harvey, W. R. 1975. Least-squares analysis of data with unequal subclass numbers. USDA, ARS H-4.

Hudson, S., M. Mullford, W. G. Whittlestone and E. Payne. 1976. Bovine plasma corticoids during parturition. J. Dairy. Sci. 59:744.

Hunter, A. G., J. K. Reneau and J. B. Williams. 1977. Factors affecting IgG concentration in day-old lambs. J. Anim. Sci. 45:1146.

Husband, A. J., M. R. Brandon and A. K. Lascelles. 1972. Absorption and endogenous production of immunoglobulins in calves. Australian J. Exp. Biol. Med. Sci. 50:491.

Husband, A. J. and A. K. Lascelles. 1975. Antibody responses to neonatal immunisation in calves. Res. Vet. Sci. 18:201.

Kelley, K. W., C. A. Osborne, J. F. Evermann, S. M. Parish and C. T. Gaskins. 1982. Effects of chronic heat and cold stressors on plasma immunoglobulin and mitogen-induced blastogenesis in calves. J. Dairy Sci. 65:293.

Klaus, G. G. B., A. Bennett and E. W. Jones. 1969. A quantitative study of the transfer of colostral immunoglobulins to the newborn calf. Immunology 16:293.

Klobasa, F. and E. Werhahn. 1981. Regulation of humoral immunity in the piglet by immunoglobulins of maternal origin. Res. Vet. Sci. 31:195.

Koch, R. M., K. E. Gregory and L. V. Cundiff. 1974. Selection in beef cattle. II. Selection response. J. Anim. Sci. 39:459.

Kruse, V. 1970. Absorption of immunoglobulin from colostrum in newborn calves. Anim. Prod. 12:627.

Logan, E. F. and T. Gibson. 1975. Serum immunoglobulin levels in suckled beef calves. Vet. Rec. 97: 229.

Logan, E. F., D. G. McBeath and B. G. Lowman. 1974. Changes in the serum immunoglobulin levels of colostrum-fed calves

during the first 12 weeks post partum. Res. Vet. Sci. 14: 394.

Logan, E. F., W. J. Penhale and R. A. Jones. 1972. Change in the serum immunoglobulin levels of colostrum-fed calves during the first 12 weeks postpartum. Res. Vet. Sci. 14:394.

Mancini, G., A. O. Carbonara and J. F. Heremans. 1965. Immunological quantitation of antigens by single radial immunodiffusion. Immunochemistry 2:235.

McBeath, D. G. and E. F. Logan. 1974. Influence of neonatal management on serum immunoglobulin levels of suckled calves. Vet. Rec. 43:466.

McGuire, T. C., N. E. Pfeiffer, J. M. Weikel and R. C. Bartsch. 1976. Failure of colostral immunoglobulin transfer in calves dying from infectious disease. J. Amer. Vet. Med. Assoc. 169:713.

Mueller, L. D. and D. K. Elleinger. 1981. Colostral immunoglobulin concentrations among breeds of dairy cattle. J. Dairy Sci. 64:1727.

Myers, L. L. 1980. Passive protection of calves against experimentally induced and naturally occurring enteric colibacillosis. Amer. Vet. Med. Assoc. 41:1952.

Norman, L. M., W. D. Hohenboken and K. W. Kelley. 1981. Genetic differences in concentration of Immunoglobulins G_1 and M in serum and colostrum of cows and in serum of neonatal calves. J. Anim. Sci. 53:1465.

Rafai, P., E. Fodor, V. L. Frenyo and E. Schultz. 1981. Effect of adrenocortical functions and microclimate on immunoglobulin absorption in calves. Acta Vet. Acad. Sci. Hung., Tomus 29:53.

Sasaki, M., C. L. Davis and B. L. Larson. 1977. Immunoglobulin IgG_1 metabolism in new born calves. J. Dairy Sci. 60:623.

Sawyer, M., C. H. Willadsen, B. I. Osburn and T. C. McGuire. 1977. Passive transfer of colostral immunoglobulins from ewe to lamb and its influence on neonatal lamb mortality. J. Amer. Vet. Med. Assoc. 171:1255.

Selman, I. E., A. D. McEwan and E. W. Fisher. 1970. Studies on natural suckling in cattle during the first eight hours post partum. I. Behavioural studies (dams). Anim. Behav. 18:265.

Selman, I. E., A. D. McEwan and E. W. Fisher. 1971a. Studies on dairy calves allowed to suckle their dams at fixed times post partum. Res. Vet. Sci. 12:1.

Selman, I. E., A. D. McEwan and E. W. Fisher. 1971b. Absorption of immune lactoglobulin by newborn dairy calves. Res. Vet. Sci. 12:205.

Stott, G. H., D. B. Marx, B. E. Menefee and G. T. Nightengale. 1979a. Colostral immunoglobulin transfer in calves. I. Period of absorption. J. Dairy Sci. 62:1632.

Stott, G. H., D. B. Marx, B. E. Menefee and G. T. Nightengale. 1979b. Colostral immunoglobulin transfer in calves. III. Amount of absorption. J. Dairy Sci. 62:1902.

Stott, G. H., D. B. Marx, B. E. Menefee and G. T. Nightengale. 1979c. Colostral immunoglobulin transfer in calves. IV. Effect of suckling. J. Dairy Sci. 62:1908.

Stott, G. H. and E. J. Reinhard. 1978. Adrenal function and passive immunity in the dystocial calf. J. Dairy Sci. 61:1457.

Watson, D. L. 1980. Immunological functions of the mammary gland and its secretion - comparative review. Australian J. Biol. Sci. 33:403.

APPENDIX

APPENDIX

Single Radial Immunodiffusion (SRID) Assay

References:

Fahey, J.L. and E.M. McKelvey. 1965. Quantitative determination of serum immunoglobulins in antibody-agar plates. J. Immunol. 94:84.

Mancini, G., A.O. Carbonara and J.F. Hermans. 1965. Immunochemical quantitation of antigens by single radial immunodiffusion. Immunochem. 2:235.

Materials:

Borate Buffer

	1L	M
-Boric acid	6.184g	.1000
-Sodium borate	9.536g	.0250
-Sodium chloride	4.384g	.0750
-Sodium azide	.200g	.0031

Place in volumetric and bring to volume by addition of distilled water.

Borate Saline Buffer

- 5 parts borate buffer
-95 parts saline (.15M)
-.02% sodium azide (.0013M)

Agar

-1.2% Noble Agar

Note: If antisera is in fluid state, it is necessary to adjust amount of buffer used. Final agar concentration must be 1.2% for best results.

Mold for Agar

-Base and cover plates 107 mm x 82 mm x 1 mm
-U-shape metal frame 1 mm thick

-7 binder clips No. 15

Pipette

-10 ml pipette
For application of agar-antibody mixture to agar mold.

Well Bore

-3 mm i.d. bore. From Miles Research Products, Miles Laboratories, Inc., Elkhart, Indiana 46515
For cutting wells in the agar.

Micropipette

-5 ul disposable Drummond Wiretrol micropipette. From Drummond Scientific Company, Broomall, Pennsylvania 19008.
For application of serum sample to agar well.

Incubator

-Incubator consists of a plastic airtight container, holding a 6 x 12 hole test tube rack on which the agar plates are placed. The container bottom is covered with approximately 1/4 inch of water.
For incubation of plates in a humid atmosphere.

Calibrated RID Viewer

-From Transidyne General Corporation,903 Airport Dr., Ann Arbor, Michigan 48106.
For measurement of immunoprecipitate rings.

Antisera

-At an appropriate dilution to cause immunoprecipitate ring diameters of < 15.0 mm.

Serum Sample

-At an appropriate dilution in borate saline buffer. Duplicates of each sample are run on the same plate.

Immunoglobulin Standards

-4 to 5 known immunoglobulin concentrations are run in duplicate on the first plate of each assay. From Miles

Research Products, Miles Laboratories, Inc., Elkhart, Indiana 46515.
For determination of immunoglobulin standard curve.

In-house Standards (IHS)

-4 known serum concentrations are run on each plate of each assay.
For determination of intra- and inter-assay coefficants of variation.

Procedure:

1. Make borate buffer and borate saline buffer.

2. Preheat water bath to 54 C.

3. Make 1.2% Noble agar solution.
Dissolve agarose in borate saline buffer by heating in pressurized cooker for 10 minutes. Place agar in the water bath until cooled to 54 C (about 5 minutes).

4. Add agar to warmed (54 C) antisera. Stir thoroughly.

5. Pipette agar-antisera mixture directly into the center of warmed molds. Approximately 8.5 ml of this solution is required to fill mold.

6. After agar has solidified (5 - 7 minutes) loosen the top edge of gel with a razor blade. Remove binder clips and slide cover plate off the agar.

7. Punch circular wells into agar with the 3 mm bore. Remove gel plugs with aspirator.

8. Apply 5 ul of the appropriate standards and diluted serum samples into each well using Wiretrol micropipettes.

9. Incubate plates in the humid atmosphere incubator for 48 hours.

10. Measure the distance of migration for each immunoprecipitate ring using the calibrated RID viewer.

11. Determine the concentration of serum samples.
Transform mg/ml concentrations of immunoglobulin standards to logrithmic values. A linear regression for these standards is computed using a log mg/ml vs. diameter units standard curve and this regression coef-

ficant is used to calculate mg/ml for the serum sample. Adjust each sample for the proper dilution factor.