Maternal and Fetal Vitamin E Concentrations and Selenium-Vitamin E Interrelationships in Dairy Cattle[1]

ROBERT J. VAN SAUN,[2] THOMAS H. HERDT AND HOWARD D. STOWE

Department of Large Animal Clinical Sciences, College of Veterinary Medicine, Michigan State University, East Lansing, MI 48824

ABSTRACT Paired dam-fetus liver and serum samples were collected from 101 pregnant dairy cattle at slaughter to determine mean fetal and maternal liver and serum vitamin E concentrations, relationships between maternal and fetal vitamin E status and interrelationships between selenium and vitamin E status. Fetal age was estimated from fetal crown-to-rump length. Fetal α-tocopherol concentration ranged from 0 to 31.4 μg/g dry wt with a mean of 7.1 μg/g dry wt and from 0 to 0.92 μg/ml with a mean of 0.29 μg/ml for liver and serum, respectively. Mean maternal liver (12.5 μg/g dry wt) and serum (2.16 μg/ml) α-tocopherol concentrations and vitamin E to cholesterol ratio (1.45) were 1.8, 7.4 and 3.5 times greater ($P < 0.0001$) than fetal means, indicating limited placental transfer of vitamin E to the fetus. Gestational age had no effect on maternal vitamin E concentration, however, fetal tissue α-tocopherol concentration declined ($P < 0.05$) with fetal age. Maternal serum α-tocopherol concentration and fetal age were found to best predict fetal α-tocopherol concentration in serum. Interrelationships between selenium and vitamin E status were minimal. These data suggest inefficient placental transfer of vitamin E, resulting in minimal protection of the neonate from vitamin E–deficiency disease as a result of prepartal maternal supplementation. *J. Nutr.* 119: 1156–1164, 1989.

INDEXING KEY WORDS:

- *vitamin E* • *selenium* • *placental transfer*
- *dairy cattle*

Placental transfer of fat soluble vitamins is believed to be limited, as suggested by equivalent or lower vitamin concentrations in the fetus compared to the dam (1). Several investigators have observed minimal placental transfer of vitamin E, with a slight increase in fetal tissue concentration with maternal supplementation (2–6). Neonatal vitamin E reserves are dependent upon colostrum intake, since colostrum tocopherol concentration exceeds that found in milk, and colostrum concentration is directly affected by maternal intake (2, 6–8). Maternal vitamin E supplementation, however, failed to completely prevent neonatal white muscle disease in lambs (9, 10).

Supplementation of either vitamin E or selenium has been shown to prevent white muscle disease in neonatal calves (10–13). The complementary preventive effect of vitamin E and selenium in vitamin E/selenium-responsive syndromes has been explained by their interrelated antioxidant functions (14). In light of probable limited placental transfer of vitamin E, emphasis has been placed on the role of selenium in perinatal deficiency syndromes.

Other studies have shown that vitamin E deficiency, even with adequate selenium, produces white muscle disease (15–17) and possibly abortion (18). Vitamin E–deficiency syndromes can also be induced through other dietary factors, such as a high concentration of dietary polyunsaturated fatty acids (PUFA), which increase the requirement for vitamin E (19, 20).

The potential for an important role of vitamin E, as well as selenium, in perinatal vitamin E/selenium-deficiency syndromes, especially abortion, warrants further investigation of maternal-fetal vitamin E relationships. In order to better establish these relationships, an investigation was initiated to determine mean tissue vitamin E concentrations of the bovine dam and fetus throughout gestation and to describe interrelationships between maternal and fetal vitamin E status. Additionally, due to the known interaction of vitamin E and selenium, interrelationships between selenium and vitamin E status within and between dam and fetus were assessed.

MATERIALS AND METHODS

On three separate occasions over a 6-mo period (May to September), paired maternal-fetal serum and liver

[1]Research presented to Michigan State University in partial fulfillment of M.S. degree.

[2]Current address and reprint requests: Department of Animal Science, 223 Morrison Hall, Cornell University, Ithaca, NY 14850

0022-3166/89 $3.00 © 1989 American Institute of Nutrition. Received 11 October 1988. Accepted 7 April 1989.

samples from dairy cattle (n = 101) were collected at an abattoir located in southwestern Michigan. Sample collection, animal descriptions and limitations of the data are as previously described (21).

Vitamin E analysis. Maternal and fetal α-tocopherol and α-tocopheryl acetate concentrations in serum and liver were assayed using an adaptation of a high pressure liquid chromatography (HPLC) procedure of Bieri, Tolliver and Catignani (22). No ester form was found in any samples, therefore vitamin E results are reported as α-tocopherol concentrations.

Liver samples were prepared by homogenizing (Polytron/Kinematica Model PT 10-35, Brinkmann Instruments, Westbury, NY) a 1.0-g liver sample in double-distilled, deionized water (*q.s.* to 5.0 ml) for 10 s. Liver homogenates were frozen (−20°C) until assayed. Liver dry weight determinations were completed on a separate 2-g sample by oven drying (70°C) to a constant weight and used to express liver α-tocopherol concentrations on a dry wt basis.

Samples of serum and liver homogenate (1 ml) were added to an equal volume of 95% ethanol to precipitate proteins. Lipid fractions were extracted with UV-grade *n*-hexane added in a 2:1 (v/v) ratio to sample and vortexed (Model S8225-1, Baxter Scientific, Romulus, MI) 2 or 5 min for serum or liver samples, respectively. Samples were then centrifuged (Model 51099H, International Equipment, Needham Heights, MA) at 1790 × *g* for 10 min, after which the hexane layer was pipetted off and filtered through 0.45-μm filter paper (Millipore, Bedford, MA).

The HPLC system consisted of a model M-45 pump, model 440 absorbance detector, model 710-B Waters Intelligent Sample processor (WISP) and model 730 data module (Millipore/Waters, Milford, MA). An extract sample (100 μl) was chromatographed on a normal phase silica column (3.9 mm i.d. × 15 cm) (Millipore/Waters, Milford, MA) with a pump flow rate of 1.1 ml/min and absorbance detection at 280 nm. The mobile phase consisted of degassed *n*-hexane and chloroform in an 85:15 (v/v) ratio.

Peaks were identified and quantified using external standards of *dl*-α-tocopherol and *dl*-α-tocopheryl acetate (Sigma Chemical, St. Louis, MO). An internal standard of *dl*-α-tocopherol was added to liver samples; 97% of the material was recovered. Sensitivity of the HPLC system was < 0.1 μg/ml of serum or hepatic extract. Due to differences in hepatic dry wt between dam and fetus, maternal and fetal liver α-tocopherol concentrations of 0 μg/g dry wt are believed to represent concentrations < 1.5 and < 2.5 μg/g dry wt, respectively. Maternal and fetal serum and liver α-tocopherol concentrations are reported as μg/ml and μg/g dry wt, respectively.

Cholesterol analysis. Maternal and fetal serum total cholesterol was determined spectrophotometrically (Model 920, Gilford Instruments, Oberlin, OH) at 500 nm using a commercial diagnostic kit (Sigma Diagnostics No. 351, St. Louis, MO). This procedure was modified, in that sample volume was increased from 10 μl to 100 μl, and 1.0 ml of double-distilled, deionized water was added to the reaction mixture to maintain a linear standard curve. Bovine serum and cholesterol standard (Sigma) were used as controls. Maternal and fetal total serum cholesterol results are reported as mg/ml.

Selenium analysis. Tissue selenium concentration and whole blood glutathione peroxidase (GSH-Px) activity, used in determining vitamin E-selenium interactions, were determined as previously described (21).

Statistical analysis. Means, Pearson correlation coefficients, analysis of variance (ANOVA) by general linear model and regression analyses were performed using Statistical Analysis System software (SAS Institute, Raleigh, NC). All analyses were not completed for every sample, due to either insufficient sample size or inability to match dam to fetal samples. Comparisons of maternal and fetal means were determined using a grouped *t*-test, due to missing values. Differences between collection time or gestational age means were compared by Tukey's test, where ANOVA indicated differences among means. As a result of large variations in individual means, differences between individual maternal or fetal means by gestational age could not be determined. Therefore, maternal and fetal measures by gestational age were grouped by trimester and compared by Tukey's test where indicated. In most instances, insufficient numbers were available for comparison of trimester 1 to other trimester means. Results reported in text, tables and figures are means ± SEM, unless otherwise indicated.

RESULTS

Vitamin E concentration. Maternal vitamin E status was not affected ($P > 0.2$) by collection time (data not shown). Fetal liver and serum α-tocopherol concentrations and serum total cholesterol were influenced ($P < 0.05$) by time of collection (data not shown). This collection period effect may be the result of herd, breed or seasonal effects, although this effect may also be confounded by a significant interaction between fetal age and collection time.

Maternal and fetal means for vitamin E and cholesterol concentrations and the ratio of vitamin E to cholesterol are presented in **Table 1**. All maternal means were greater ($P < 0.0001$) than corresponding fetal values, with mean maternal liver (12.5 ± 1.1 μg/g dry wt) and serum (2.16 ± 0.15 μg/ml) α-tocopherol concentrations and vitamin E/cholesterol ratio (1.45 ± 0.1) being 1.8, 7.4 and 3.5 times greater than corresponding fetal means (7.1 ± 0.72 μg/g dry wt, 0.29 ± 0.02 μg/ml, 0.42 ± 0.03, respectively). Mean maternal serum total cholesterol (1.44 ± 0.05 mg/ml) was 2.0 times greater ($P < 0.0001$) than mean fetal serum cholesterol (0.73 ± 0.03 mg/ml).

TABLE 1

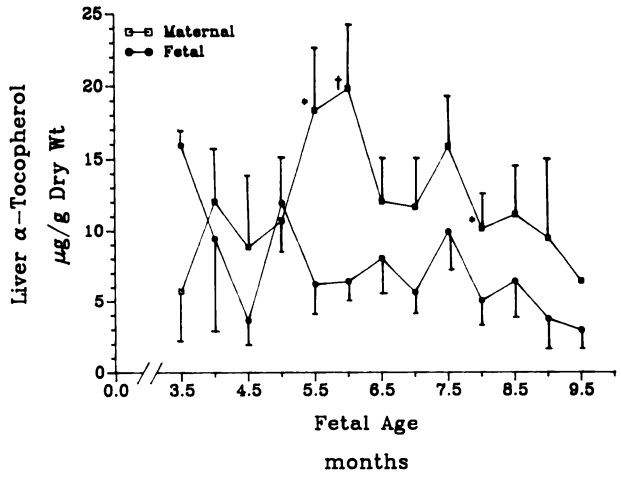
Mean bovine maternal and fetal tissue vitamin E and serum cholesterol concentrations and vitamin E to cholesterol ratios[1]

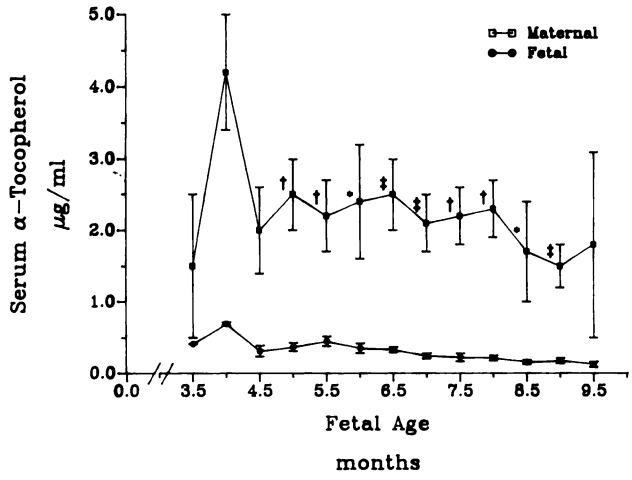
Tissue	Maternal	Fetal	*P*-value
Liver vitamin E, *μg/g dry wt*	12.5 ± 1.1 (99)	7.1 ± 0.72 (97)	0.0001
Serum vitamin E, *μg/ml*	2.16 ± 0.15 (82)	0.29 ± 0.02 (93)	0.0001
Total cholesterol, *mg/ml*	1.44 ± 0.05 (71)	0.73 ± 0.03 (79)	0.0001
Ratio[2]	1.45 ± 0.10 (67)	0.42 ± 0.03 (75)	0.0001

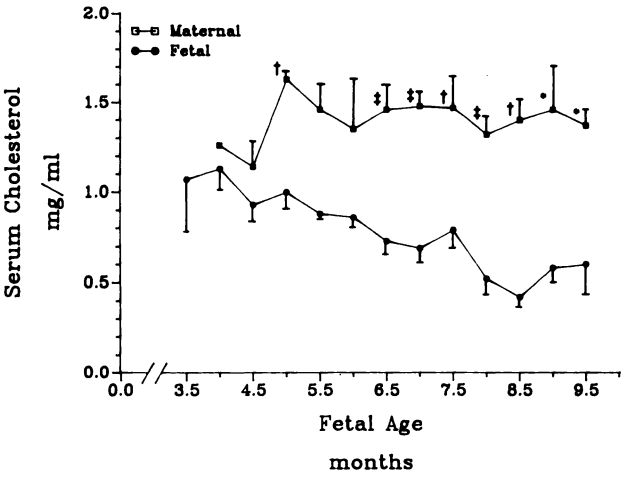
[1]Values are means ± SEM; number of animals is in parentheses.
[2]Serum vitamin E/cholesterol ratio (μg/ml:mg/ml)

Maternal liver α-tocopherol concentration was variable in early gestation, rose to a peak value at 6 mo and then declined with fetal age (**Fig. 1*A***). Fetal hepatic α-tocopherol concentration was also variable in early gestation and then gradually declined as gestation proceeded. Maternal hepatic α-tocopherol concentration was not affected by fetal age; however, fetal values tended ($P < 0.16$) to decline. Maternal liver α-tocopherol concentration was greater ($P < 0.0005$, 0.004) than the fetal mean in trimester 2 and 3 (**Fig. 2*A***). Fetal liver α-tocopherol concentration differed ($P < 0.05$) from trimester 1 to 3. Maternal means were not different ($P < 0.39$) between trimesters.

Maternal serum α-tocopherol concentration was consistently greater than mean fetal serum α-tocopherol concentration throughout gestation ($P < 0.05$–0.001, **Fig. 1*B***) or grouped by trimester ($P < 0.0001$, **Fig. 2*B***). Maternal serum α-tocopherol concentration was not







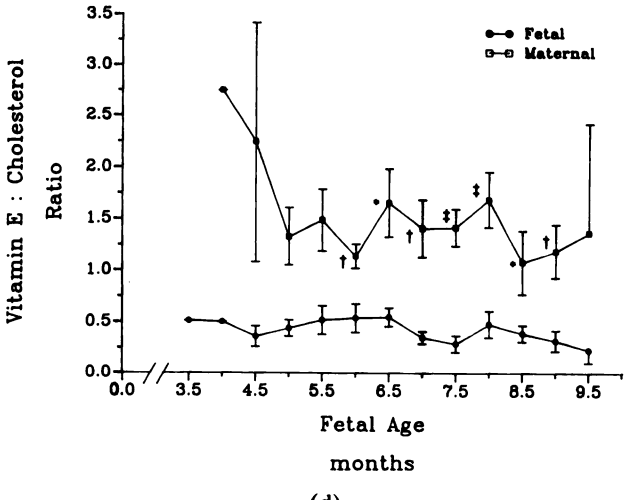


FIGURE 1 Bovine maternal (□) and fetal (●) mean α-tocopherol concentrations in liver (***A***) and serum (***B***), serum total cholesterol (***C***) and vitamin E to cholesterol ratio (***D***) during gestation. Each point represents a mean ± SEM for 1–13 animals. Maternal-fetal mean comparison: *$P < 0.05$, †0.01, ‡0.001.

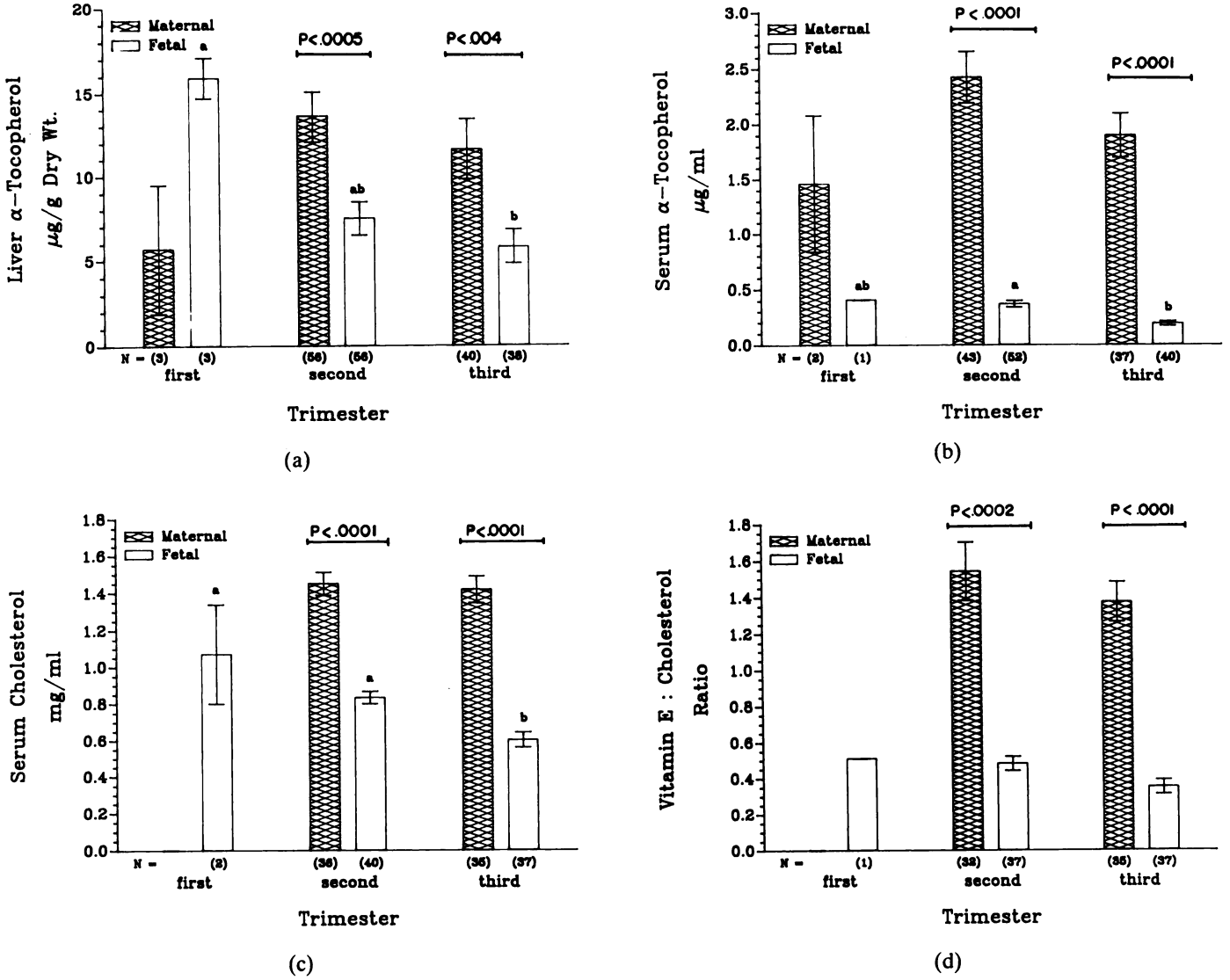


FIGURE 2 Bovine maternal (shaded) and fetal (open) mean α-tocopherol concentrations in liver (***A***) and serum (***B***), serum total cholesterol (***C***) and vitamin E to cholesterol ratio (***D***), by gestational trimester. [ab]Maternal or fetal means with different superscript letters differ significantly ($P < 0.05$). *P*-value for maternal-fetal grouped *t*-test is shown above each trimester.

affected ($P < 0.7$) by fetal age. Mean fetal serum α-tocopherol declined ($P < 0.0001$) with fetal age. Mean serum α-tocopherol concentration by trimester was not different ($P = 0.17$) for the dam, but declined ($P < 0.05$) from trimester 2 to 3 in the fetus.

Mean maternal serum total cholesterol concentration was consistently greater ($P < 0.05–0.001$) than the fetal mean throughout gestation (**Fig. 1*C***) and was greater ($P < 0.0001$) than the fetal mean in trimester 2 and 3 (**Fig. 2*C***). Maternal cholesterol concentration was not affected by fetal age, whereas fetal values declined ($P < 0.0001$). Mean maternal cholesterol concentration was not different between trimester 2 and 3; however, mean fetal cholesterol concentration in trimester 3 was less ($P < 0.05$) than means for trimester 1 and 2 (Fig. 2*C*).

The maternal vitamin E/cholesterol ratio was also consistently greater than the fetal ratio across gestation ($P < 0.05–0.001$, **Fig. 1*D***) and in trimester 2 ($P < 0.0002$) and 3 ($P < 0.0001$, **Fig. 2*D***). Neither the maternal nor fetal vitamin E/cholesterol ratio was influenced by fetal age. The mean fetal vitamin E/cholesterol ratio tended ($P = 0.09$) to decline by trimester.

Maternal-fetal interrelationships. Multiple correlation analyses using measured variables for dam and fetus are shown in **Table 2**. Liver vitamin E concentration was correlated with serum vitamin E ($r = 0.21$, $P < 0.06$) in the dam and negatively correlated to crown-to-rump length ($r = -0.21$, $P < 0.04$) in the fetus. Maternal and fetal serum vitamin E concentrations were positively correlated ($P < 0.0001$) to both serum cholesterol ($r = 0.44, 0.45$) and the vitamin E/cholesterol ratio ($r = 0.86, 0.67$), respectively. Fetal serum cholesterol tended ($P = 0.06$) to be associated negatively ($r = -0.22$) with the vitamin E/cholesterol ratio. Fetal crown-to-rump length was related negatively to fetal

liver and serum ($r = -0.53$, $P < 0.0001$) α-tocopherol concentrations, serum cholesterol ($r = -0.62$, $P < 0.0001$) and the vitamin E/cholesterol ratio ($r = -0.22$, $P < 0.06$).

Correlations between maternal and fetal estimators of vitamin E status and cholesterol concentration are shown in **Table 3**. Fetal serum vitamin E concentration and the vitamin E/cholesterol ratio were related to maternal liver ($r = 0.23$, $P < 0.03$; $r = 0.25$, $P < 0.03$) and serum ($r = 0.32$, $P < 0.005$; $r = 0.32$, $P < 0.01$) vitamin E concentrations and the vitamin E/cholesterol ratio ($r = 0.33$, $P < 0.009$; $r = 0.32$, $P < 0.02$), respectively. Maternal serum vitamin E concentration tended ($P = 0.09$) to be related negatively ($r = -0.19$) to fetal crown-to-rump length.

Prediction model. Fetal age accounted for a greater proportion of the variation in fetal serum α-tocopherol than any measure of maternal vitamin E status. Fetal liver α-tocopherol concentration could not be predicted ($R^2 < 0.10$) from any single or multiple variable of the dam's vitamin E status. A multiple linear regression model ($R^2 = 0.31$, $P < 0.0001$) was derived from regressing fetal serum α-tocopherol concentration on fetal age ($t = -4.7$, $P < 0.0001$) and maternal serum α-tocopherol concentration ($t = 2.2$, $P < 0.03$). Using the maternal vitamin E/cholesterol ratio in place of maternal serum α-tocopherol concentration produces a similar model ($R^2 = 0.32$, $P < 0.0001$). A graphic presentation of this model, given by the equation $Y = 0.63 + 0.03$*MSVE $- 0.06$*FAGE, where MSVE is maternal serum α-tocopherol concentration (μg/ml) and FAGE is fetal age in months, is shown in **Figure 3**.

This model predicts decreasing fetal serum vitamin E concentration with increasing fetal age, and increasing fetal vitamin E status with greater maternal vitamin E concentration. In addition, less of a decline in fetal serum vitamin E concentration with gestation is predicted in fetuses from vitamin E–adequate dams (maternal serum α-tocopherol > 2 μg/ml), compared to vitamin E–depleted (< 2 μg/ml) dams.

Selenium–vitamin E interrelationships. Multiple correlations between various estimators of selenium and vitamin E status were determined for the dam and fetus (**Table 4**) and between dam and fetus (**Table 5**). In the dam, serum cholesterol concentration was related to the selenium concentration in liver ($r = 0.22$, $P < 0.07$), serum ($r = 0.31$, $P < 0.008$), erythrocyte ($r = 0.33$, $P < 0.03$) and whole blood ($r = 0.32$, $P < 0.03$). In the fetus, serum selenium concentration was negatively correlated to serum vitamin E ($r = -0.34$, $P < 0.001$) and cholesterol ($r = -0.34$, $P < 0.002$) concentrations.

Maternal serum selenium concentration was negatively correlated with fetal serum vitamin E concentration ($r = -0.20$, $P < 0.06$) and the vitamin E/cholesterol ratio ($r = -0.25$, $P < 0.04$). Maternal serum vitamin E concentration was negatively correlated with fetal whole blood GSH-Px activity ($r = -0.69$, $P < 0.009$) and tended ($P < 0.1$) to be correlated negatively

TABLE 2

Correlations between various estimators of vitamin E (vit E) status and cholesterol concentrations and between estimators of vitamin E status, cholesterol concentrations and fetal crown-to-rump (C-R) length for the pregnant dairy cow and fetus[1]

Variables	Maternal	Fetal
Liver vit E–Serum vit E	0.211 (0.06)	0.009 (0.93)
Liver vit E–Cholesterol	0.207 (0.08)	0.190 (0.10)
Liver vit E–Ratio[2]	0.182 (0.14)	0.084 (0.48)
Liver vit E–C-R length	—	−0.207 (0.04)
Serum vit E–Cholesterol	0.444 (0.0002)	0.448 (0.0001)
Serum vit E–Ratio	0.864 (0.0001)	0.674 (0.0001)
Serum vit E–C-R length	—	−0.531 (0.0001)
Cholesterol–Ratio	0.006 (0.96)	−0.219 (0.06)
Cholesterol–C-R length	—	−0.618 (0.0001)
Ratio–C-R length	—	−0.215 (0.06)

[1]Values are Pearson correlation coefficients, with *P*-values in parentheses.
[2]Serum vitamin E/cholesterol ratio (μg/ml:mg/ml).

TABLE 3

Correlations between bovine maternal and fetal tissue vitamin E and cholesterol concentrations, vitamin E to cholesterol ratio and fetal crown-to-rump (C-R) length[1]

	Maternal variables			
Fetal variables	Liver vitamin E	Serum vitamin E	Serum cholesterol	Ratio[2]
Liver vitamin E	0.149 (0.15)	0.008 (0.94)	0.220 (0.07)	−0.051 (0.69)
Serum vitamin E	0.234 (0.03)	0.318 (0.005)	0.076 (0.54)	0.326 (0.009)
Serum cholesterol	−0.0003 (1.0)	−0.015 (0.90)	0.066 (0.63)	−0.161 (0.25)
Ratio[2]	0.254 (0.03)	0.321 (0.01)	0.028 (0.84)	0.323 (0.02)
C-R length	−0.069 (0.49)	−0.186 (0.09)	−0.036 (0.76)	−0.154 (0.21)

[1]Values are Pearson correlation coefficients, with *P*-values in parentheses.
[2]Serum vitamin E/cholesterol ratio (μg/ml:mg/ml).

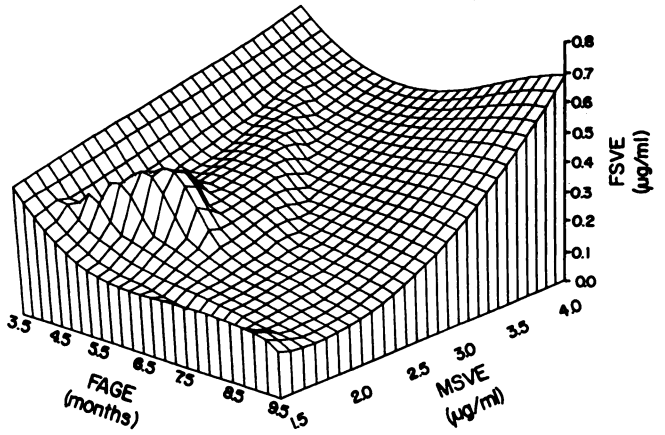


FIGURE 3 Relationship between bovine fetal serum α-tocopherol concentration (FSVE) and fetal age (FAGE) and maternal serum α-tocopherol concentration (MSVE). (Regression equation: $Y = 0.63 + 0.03\text{MSVE} - 0.06\text{FAGE}$, where MSVE is expressed in μg/ml and FAGE in months).

($r = -0.19$) to serum selenium concentration and positively ($r = 0.20$) to liver selenium concentration. Fetal whole blood GSH-Px activity was also negatively correlated ($r = -0.64$) with the maternal vitamin E/cholesterol ratio ($P < 0.01$). The maternal vitamin E/cholesterol ratio was negatively correlated to fetal selenium concentration in serum ($r = -0.28$, $P < 0.03$) and whole blood ($r = -0.26$, $P < 0.09$).

DISCUSSION

Concentrations of α-tocopherol in serum of the dams were in the range of previously reported values for deficiency and adequacy (23–26). McMurray and Rice (27) reported serum α-tocopherol concentrations of 1.0–1.5 μg/ml to be associated with clinical lesions of white muscle disease, with values < 0.2 μg/ml considered severely deficient. Bayfield and Mylrea suggested > 4.0 μg/ml to be an adequate serum vitamin E concentration in adult cattle (24). Maternal serum α-tocopherol concentrations (range: 0.19–7.05 μg/ml, mean: 2.16 μg/ml) were consistent with reported values of 1.65 μg/ml (23), 1.4 to 3.1 μg/ml (25) and 0.91 to 2.32 μg/ml (28) for adult animals receiving no vitamin E supplementation. Pehrson and Hakkarainen (26) reported a serum total tocopherol concentration of 4.11–5.20 μg/ml for lactating and 2.52–3.75 μg/ml for dry cows receiving 5–10 mg vitamin E per kg of concentrates daily.

Diet (25, 26, 28, 29) and season (28) effects on vitamin E status (silage diets > hay diets; fall > winter) have been reported in cattle. Data from the current study found no differences in mean maternal tocopherol concentrations in liver or serum over a collection time of May to September; however, means from collection periods in August and September were greater than those from May for both liver and serum tocopherol concentrations (data not shown).

TABLE 4

***Correlations between selenium (Se) and vitamin E variables in the pregnant dairy cow and fetus*[1]**

Vitamin E variables	Selenium variables				
	Liver Se	Serum Se	Erythrocyte Se	Whole blood Se	GSH-Px activity[2]
			Maternal		
Liver vitamin E	0.122	0.115	0.101	0.113	0.146
	(0.23)	(0.28)	(0.44)	(0.39)	(0.26)
Serum vitamin E	0.029	−0.058	−0.072	−0.104	−0.056
	(0.79)	(0.61)	(0.60)	(0.45)	(0.69)
Serum cholesterol	0.220	0.312	0.328	0.324	0.222
	(0.07)	(0.008)	(0.03)	(0.03)	(0.14)
Ratio[3]	−0.134	−0.174	−0.163	−0.202	−0.103
	(0.28)	(0.16)	(0.31)	(0.21)	(0.52)
			Fetal		
Liver vitamin E	0.073	−0.085	−0.024	−0.024	−0.034
	(0.48)	(0.42)	(0.85)	(0.84)	(0.86)
Serum vitamin E	0.102	−0.336	0.146	0.058	0.007
	(0.34)	(0.001)	(0.25)	(0.64)	(0.97)
Serum cholesterol	−0.068	−0.344	−0.048	−0.113	−0.188
	(0.57)	(0.002)	(0.73)	(0.42)	(0.38)
Ratio[3]	0.021	−0.018	0.195	0.191	0.186
	(0.86)	(0.88)	(0.18)	(0.18)	(0.41)

[1]Values are Pearson correlation coefficients, with *P*-values in parentheses.
[2]Whole blood gluthathione peroxidase activity.
[3]Serum vitamin E/cholesterol ratio (μg/ml:mg/ml).

TABLE 5

Correlations between bovine maternal and fetal selenium (Se) and vitamin E variables[1]

	Selenium variables				
	Liver Se	Serum Se	Erythrocyte Se	Whole blood Se	GSH-Px activity[2]
Fetal vitamin E variables			Maternal		
Liver vitamin E	0.055	−0.055	−0.109	−0.113	−0.083
	(0.59)	(0.61)	(0.41)	(0.39)	(0.53)
Serum vitamin E	0.000	−0.203	0.038	−0.036	−0.088
	(1.00)	(0.06)	(0.78)	(0.79)	(0.51)
Serum cholesterol	0.012	0.065	0.200	0.203	0.234
	(0.91)	(0.59)	(0.18)	(0.18)	(0.11)
Ratio[3]	0.091	−0.246	−0.156	−0.228	−0.229
	(0.44)	(0.04)	(0.32)	(0.14)	(0.14)
Maternal vitamin E variables			Fetal		
Liver vitamin E	0.103	−0.034	0.086	0.024	0.121
	(0.32)	(0.75)	(0.48)	(0.84)	(0.54)
Serum vitamin E	0.204	−0.194	−0.092	−0.157	−0.693
	(0.07)	(0.09)	(0.52)	(0.25)	(0.009)
Serum cholesterol	0.137	0.055	−0.035	0.005	−0.641
	(0.27)	(0.66)	(0.82)	(0.97)	(0.01)
Ratio[3]	0.027	−0.279	−0.133	−0.263	−0.351
	(0.83)	(0.03)	(0.42)	(0.09)	(0.26)

[1]Values are Pearson correlation coefficients, with *P*-values in parentheses.
[2]Whole blood glutathione peroxidase.
[3]Serum vitamin E/cholesterol ratio (μg/ml:mg/ml).

Vitamin E is a component of serum lipoprotein, and thus its concentration in serum can be expected to vary with lipoprotein concentration. Serum vitamin E concentration is frequently expressed as a ratio with serum lipid or lipoproteins, because of this relationship (30). In the present study, this relationship was confirmed, since both dam and fetus had equivalent correlations (r = 0.44 vs. 0.45, $P < 0.0005$) between serum α-tocopherol and cholesterol concentrations, even though the maternal mean vitamin E/cholesterol ratio (1.45) was greater ($P < 0.0001$) than the fetal ratio (0.42). Maternal vitamin E/cholesterol ratios from the present study were in agreement with reported values of 0.95–1.5 mg/g (26), accounting for differences between total lipid and cholesterol concentrations.

References in the literature citing α-tocopherol concentrations in liver of adult cattle are extremely limited. Data accumulated over the past 5 yr at the Michigan State University Animal Health Diagnostic Laboratory suggest a concentration > 15 μg/g liver dry wt to be adequate (unpublished data). Concentrations obtained in the current study ranged from deficient to adequate (0–47 μg/g dry wt) with the maternal mean (12.5 μg/g dry wt) considered marginally adequate.

A significant decline in fetal liver and serum α-tocopherol concentrations with fetal age, in addition to negative correlations between fetal vitamin E status and crown-to-rump length, suggest possibly a decreasing efficiency in placental vitamin E transfer as gestation proceeds. Alternatively, this decline in fetal vitamin E status may be the result of a dilution effect as a result of rapid fetal growth with no change in transfer efficiency. A third hypothesis is that less vitamin E from the maternal placental transfer pool is available during the period of rapid fetal growth. Our data do not support this third hypothesis, since maternal vitamin E status is not influenced by gestational age.

The fetal vitamin E/cholesterol ratio did not decline with fetal age and, along with fetal liver α-tocopherol concentration, was not as negatively correlated with crown-to-rump length as was serum α-tocopherol concentration. This would suggest that the decline in fetal serum vitamin E concentration may better reflect the decline in serum cholesterol concentration, rather than a substantial decline in fetal serum vitamin E status as gestation proceeds. Possibly, the vitamin E/cholesterol ratio is a more appropriate measure of fetal vitamin E status.

Our data indicate a limited ability of α-tocopherol to cross the placenta, as evidenced by fetal concentrations being substantially less ($P < 0.0001$) than corresponding maternal values. This is consistent with findings from other investigations (2–4, 6) and is in contrast to findings for maternal-fetal comparisons for selenium placental transfer (21). Our data would suggest adequate maternal prepartum supplementation of selenium, rather than vitamin E, would be more effective in preventing neonatal white muscle disease. With limited placental

transfer of vitamin E, neonatal calves rely heavily on the ingestion of colostrum as their source of vitamin E (4, 7, 8). Investigators have reported white muscle disease lesions in suckling and weanling lambs with adequate selenium status, but deficient in vitamin E, suggesting inadequate colostrum intake, colostral vitamin E concentration (due to maternal deficiency) or vitamin E supplementation postnatally (15, 16).

However, Yamini and Mullaney (18) have postulated that vitamin E deficiency may play a potential role in abortion. They reported vitamin E and selenium concentrations in 74 aborted bovine fetuses. These aborted fetuses were classified as idiopathic abortion, since no infectious or other potential abortifacient agent was determined. Undetectable concentrations of vitamin E were found in 27% (20/74) of the aborted fetuses, and 45% (9/20) had histological lesions consistent with white muscle disease (18). Corresponding hepatic selenium concentrations in these aborted fetuses ranged from 0.3 to 1.58 μg/g dry wt.

Comparisons of vitamin E and selenium concentrations were made between the data from aborted bovine fetuses (18) and fetuses from the present study, since all assays were performed in the same laboratory. In aborted fetuses, hepatic α-tocopherol concentration ranged from 0 to 35 μg/g dry wt, with a mean of 7.1 μg/g dry wt. In our data, fetal hepatic α-tocopherol concentration ranged 0–31.4 μg/g dry wt, with a mean of 7.1 μg/g dry wt. These comparisons reveal minimal differences in liver α-tocopherol content between aborted fetuses (18) and fetuses from the present study. Analysis of serum α-tocopherol concentration of the aborted fetuses was not performed. In contrast, hepatic selenium concentration in aborted fetuses was substantially less than fetuses from the present study (21). This might suggest that selenium, rather than vitamin E, plays a more important role in protecting the fetus from increased free radical (oxidant) load associated with potential abortion-inducing lesions.

Our data also indicate fetal vitamin E status can be influenced by maternal vitamin E status, suggesting some placental transfer. Comparing fetal α-tocopherol concentration in liver and serum and the vitamin E/cholesterol ratio from vitamin E–deplete or –adequate dams from the present study reveals that fetal serum α-tocopherol concentration, but not liver concentration, and the vitamin E/cholesterol ratio are affected by maternal vitamin E status. This is in agreement with other reports (8). When fetuses from the present study were grouped in terms of vitamin E status (liver, serum or the vitamin E/cholesterol ratio) of their dams, fetal liver α-tocopherol concentration had a mean of 32 and 110% of the maternal liver concentration from vitamin E–adequate (> 15 μg/g dry wt) and –deplete (< 15 μg/g dry wt) dams, respectively. However, mean hepatic α-tocopherol concentration comparing these two fetal groups (adequate: 8.2; deplete: 6.5 μg/g dry wt) was not statistically different ($P > 0.05$). Fetal serum α-tocopherol concentration and the vitamin E/cholesterol ratio means from vitamin E–adequate (serum: > 2.0 μg/ml; ratio: > 1.5) and –deplete (serum: < 2.0 μg/ml; ratio: < 1.5) dams represented 10 and 20% and 24.5 and 36.7% of the maternal concentration, respectively. Mean fetal serum α-tocopherol concentration (0.33 vs. 0.24 μg/ml) and the vitamin E/cholesterol ratio (0.52 vs. 0.35) were greater ($P < 0.05$) from vitamin E–adequate, compared to –deplete dams, respectively. These data suggest a fetal vitamin E concentrating ability during maternal vitamin E deficiency.

Predicting fetal vitamin E status from maternal concentrations would be beneficial for evaluating the potential presence of vitamin E–responsive perinatal disease. Fetal liver α-tocopherol concentration < 2.0 μg/g dry wt has been associated with white muscle disease and abortion (18); however, no relationship between fetal liver and maternal α-tocopherol concentration was revealed by the present study. A model predicting fetal serum α-tocopherol concentration, based on fetal age and maternal serum α-tocopherol concentration, was derived. The relationship of fetal serum α-tocopherol concentration to disease is unknown. In addition, the observed narrow range in fetal values (0–1.0 μg/ml) makes application of this model limited. Perhaps other fetal tissues containing elevated concentrations of vitamin E, such as adrenals, platelets, kidneys and pancreas, may be better indicators of fetal vitamin E status than serum (4).

The integrated functional roles of vitamin E and selenium as antioxidants has led to a suggested interaction between these nutrients. No interaction between vitamin E and selenium, in facilitating the absorption of the other, has been found (31–33). Few studies have investigated potential interaction in placental transfer of vitamin E and selenium. Cheeke, Bull and Oldfield (34) observed that selenium supplementation decreased ($P < 0.005$) placental transfer of α-tocopherol in rats. Stowe et al. (33) observed that serum selenium concentration in precolostrum-fed calves from vitamin E– and selenium–supplemented dams was greater ($P < 0.01$) than that of calves from either vitamin E– or selenium–supplemented dams. No difference in precolostrum-fed calf serum α-tocopherol concentration was seen with these same treatments.

In the present study, minimal interactions between selenium and vitamin E measures were found in the dam or fetus. Fetal serum selenium was negatively correlated ($r = -0.34$, $P < 0.001$) to fetal serum vitamin E concentration, but not to the vitamin E/cholesterol ratio. A similar negative trend was revealed between maternal and fetal serum selenium concentrations and serum vitamin E concentration ($r = -0.2$, $P < 0.1$) and the vitamin E/cholesterol ratio ($r = -0.25$, $P < 0.05$). Fetal whole blood GSH-Px activity was also correlated negatively ($r = -0.69$, $P < 0.009$) with maternal serum vitamin E concentration. These results would support the suggestion by Cheeke, Bull and Oldfield (34) that

selenium spared the requirement of vitamin E in the fetus. Further investigation into fetal vitamin E requirements, relationships to maternal status and interrelationships with selenium are suggested from this study in an effort to better understand the pathogenesis of perinatal vitamin E/selenium–responsive disease.

ACKNOWLEDGMENTS

The authors thank A. House and T. Thiel for their assistance in the α-tocopherol analyses, and M. E. Shea for preparation of the figures.

LITERATURE CITED

1. Malone, J. I. (1975) Vitamin passage across the placenta. *Clin. Perinatol.* 2: 295–307.
2. Mason, K. E. & Bryan, W. L. (1940) Placental and mammary transfer of vitamin E in the rat. *J. Nutr.* 20: 501–517.
3. Parrish, D. B., Wise, G. H., Latschar, C. E. & Hughes, J. S. (1950) Effect of the prepartal diet of the cow on the placental and mammary transfer of tocopherols to the calf. *J. Nutr.* 40: 193–202.
4. Hidiroglou, M., Hoffman, I. & Jenkins, K. J. (1969) Selenium distribution and radiotocopherol metabolism in the pregnant ewe and fetal lamb. *Can. J. Physiol. Pharmacol.* 47: 953–962.
5. Mino, M. & Nishino, H. (1973) Fetal and maternal relationship in serum vitamin E level. *J. Nutr. Sci. Vitaminol.* 19: 475–482.
6. Martin, M. M. & Hurley, L. S. (1977) Effects of large amounts of vitamin E during pregnancy and lactation. *Am. J. Clin. Nutr.* 30: 1629–1637.
7. Parrish, D. B., Wise, G. H. & Hughes, J. S. (1947) Properties of the colostrum of the dairy cow. I. Tocopherol levels in the colostrum and in the early milk. *J. Dairy Sci.* 30: 849–860.
8. Whiting, F. & Loosli, J. K. (1948) The placental and mammary transfer of tocopherols (vitamin E) in sheep, goats and swine. *J. Nutr.* 36: 721–726.
9. Proctor, J. F., Hogue, D. E. & King, J. M. (1959) The effect of oral administration and maternal transfer of selenium and vitamin E on the incidence of muscular dystrophy in lambs. *J. Anim. Sci.* 18: 1525 (abs).
10. Hogue, D. E., Proctor, J. F., Warner, R. G. & Loosli, J. K. (1962) Relation of selenium, vitamin E and an unidentified factor to muscular dystrophy (stiff-lamb or white muscle disease) in the lamb. *J. Anim. Sci.* 21: 25–29.
11. Vawter, L. R. & Records, E. (1947) Muscular dystrophy (white muscle disease) in young calves. *J. Am. Vet. Med. Assoc.* 110: 152–157.
12. Safford, J. W., Swingle, K. F. & Marsh, H. (1954) Experimental tocopherol deficiency in young calves. *Am. J. Vet. Res.* 15: 373–384.
13. Muth, O. H., Oldfield, J. E., Remmert, L. F. & Schubert, J. R. (1958) Effects of selenium and vitamin E on white muscle disease. *Science* 128: 1090.
14. Hoekstra, W. G. (1975) Biochemical function of selenium and its relation to vitamin E. *Fed. Proc.* 34: 2083–2089.
15. Steele, P., Peet, R. L., Skirrow, S., Hopkinson, W. & Masters, H. G. (1980) Low alpha-tocopherol levels in livers of weaner sheep with nutritional myopathy. *Aust. Vet. J.* 56: 529–532.
16. Maas, J. P., Bulgin, M. S., Anderson, B. C. & Frye, T. M. (1984) Nutritional myodegeneration associated with vitamin E deficiency and normal selenium status in lambs. *J. Am. Vet. Med. Assoc.* 184: 201–204.
17. Whanger, P. D., Weswig, P. H., Schmitz, J. A. & Oldfield, J. E. (1977) Effects of selenium and vitamin E deficiencies on reproduction, growth, blood components and tissue lesions in sheep fed purified diets. *J. Nutr.* 107: 1288–1297.
18. Yamini, B. & Mullaney, T. P. (1985) Vitamin E and selenium deficiency as a possible cause of abortion in food animals. *Proc. 28th Annual Meeting Am. Assoc. Vet. Lab. Diagnosticians*, pp. 131–144.
19. Dam, H. (1962) Interrelationships between vitamin E and polyunsaturated fatty acids in animals. *Vitam. Horm.* 20: 527–540.
20. Michel, R. L., Makdani, D. D., Huber, J. T. & Sculthorpe, A. E. (1972) Nutritional myopathy due to vitamin E deficiency in calves fed fish protein concentrate as the sole source of protein. *J. Dairy Sci.* 55: 498–506.
21. Van Saun, R. J., Herdt, T. H. & Stowe, H. D. (1989) Maternal and fetal selenium concentrations and their interrelationships in dairy cattle. *J. Nutr.* 119: 1128–1137.
22. Bieri, J. G., Tolliver, T. J. & Catignani, G. L. (1979) Simultaneous determination of alpha-tocopherol and retinol in plasma or red cells by high pressure liquid chromatography. *Am. J. Clin. Nutr.* 32: 2143–2149.
23. Lyford, S. J. & Colby, B. E. (1967) Blood tocopherol levels in beef cattle. *J. Anim. Sci.* 26: 877–878 (abs).
24. Bayfield, R. F. & Mylrea, P. J. (1969) Carotenoid and tocopherol levels in the serum of apparently healthy dairy cattle. *J. Dairy Res.* 36: 137–144.
25. Lynch, G. P. (1983) Changes in tocopherols in blood serum of cows fed hay or silage. *J. Dairy Sci.* 66: 1461–1465.
26. Pehrson, B. & Hakkarainen, J. (1986) Vitamin E status of healthy Swedish cattle. *Acta Vet. Scand.* 27: 351–360.
27. McMurray, C. H. & Rice, D. A. (1982) Vitamin E and selenium deficiency diseases. *Irish Vet. J.* 36: 57–65.
28. Schingoethe, D. J., Kirkbride, C. A., Palmer, I. S., Owens, M. J. & Tucker, W. L. (1982) Response of cows consuming adequate selenium to vitamin E and selenium supplementation prepartum. *J. Dairy Sci.* 65: 2338–2344.
29. Schingoethe, D. J., Parsons, J. G., Ludens, F. C., Tucker, W. L. & Shave, H. J. (1978) Vitamin E status of dairy cows fed stored feeds continuously or pastured during summer. *J. Dairy Sci.* 61: 1582–1589.
30. Horwitt, M. K., Harvey, C. C., Dahm, C. H. & Steach, M. T. (1972) Relationship between tocopherol and serum lipid levels for determination of nutritional adequacy. *Ann. NY Acad. Sci.* 203: 223–236.
31. Harrison, J. H. & Conrad, H. R. (1984) Selenium content and glutathione peroxidase activity in tissues of the dairy cow after short-term feeding. *J. Dairy Sci.* 67: 2464–2470.
32. Hidiroglou, M., Jenkins, H. E. & Lessard, J. R. (1970) Metabolism of vitamin E in sheep. *Brit. J. Nutr.* 24: 917–928.
33. Stowe, H. D., Thomas, J. W., Johnson, T., Marteniuk, J. V., Morrow, D. A. & Ullrey, D. E. (1988) Responses of dairy cattle to long-term and short-term supplementation with oral selenium and vitamin E. *J. Dairy Sci.* 71: 1830–1839.
34. Cheeke, P. R., Bull, R. C. & Oldfield, J. E. (1969) The role of selenium in the placental transfer of vitamin E in the rat. *Proc. Soc. Exp. Bio. & Med.* 130: 172–174.