Effect of Gestational Folic Acid Supplementation on Offspring Immune Organ Development and Postnatal Immune Response

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Summary and Implications

Pairs of littermate, primiparous sows were fed a low folic acid, basal diet for 98 days to minimize body folic acid (FA) stores. Following the depletion period, sows were synchronized and bred via artificial insemination. Feeding of experimental diets was initiated on day 1 post-breeding and was continued throughout pregnancy. Experimental diets consisted of the low folic acid, basal diet supplemented with either 0 or 8 mg of FA per sow per day. The FA supplementation elevated sow serum FA concentration during pregnancy but did not alter immunoglobulin concentration in sow serum, piglet serum nor sow colostral whey at parturition. The FA supplementation did not affect the number of pigs per litter nor litter birth weight. The FA supplementation of the gravid sow did not alter piglet thymus or spleen weight, DNA, or protein content at birth, but resulted in a lower ($P<.01$) percentage of CD2+ lymphocytes in blood of pigs post-weaning. Pigs from FA supplemented sows also exhibited a greater ($P<.05$) secondary antibody response to sheep red blood cells.

Based on these data, FA status of the gravid sow influences serum FA concentrations of the dam and postnatal immune response of the offspring.

Introduction

Economically important goals in swine production include the production of healthy, viable offspring that grow muscle tissue rapidly and produce highly muscled carcasses. Numerous environmental factors, including the dam's nutritional status, influence whether the offspring will survive and what proportion of an offspring's genetic capacity for growth will be expressed both pre- and postnatally. It has been demonstrated that both postnatal growth (2) and immune capacity (1) of mammals can be affected by prenatal growth.

Folic acid has a fundamental role in denovo synthesis of DNA. Therefore, the amount of FA available to the sow at critical times during pregnancy can determine the amount of hyperplastic growth (DNA accretion) of fetal and placental tissues as well as proliferation of immunoglobulin-producing cells. It has been demonstrated that serum folic acid levels decline during pregnancy in sows to minimal levels during mid-pregnancy (3). It also has been shown that the rate of FA catabolism increases during pregnancy in the rat (4). These findings would support the hypothesis that the FA requirement is increased during pregnancy, presumably to support the rapid rate of DNA synthesis in both fetal and maternal tissues.

The objective of this experiment was to determine the influence of dietary FA supplementation during pregnancy in sows on the immune capacity and subsequent performance of the offspring.

Materials and Methods

Nineteen pairs of littermate primiparous sows from a single genetic strain (moderate lean growth) and source of origin were utilized for this experiment. In an effort to ensure uniform and minimal FA stores, all sows were put on a low folic acid regimen for 98 days prior to breeding. During this period, sows were fed 1.9 kg/day of a low FA, basal diet (.28 mg of FA/kg diet) (Table 1). The basal diet consisted of a corn/casein mixture supplemented with minerals and vitamins (except folic acid) at levels that exceeded the gravid sow's estimated nutrient needs (5).

Table 1. Dietary feeding regimens.

Stage	Diet	Analyzed FA[a], mg/kg	Feed offered
Prebreeding	Basal	.28	1.9 kg/d
Pregnancy	Basal (-FA)	.28	1.9 kg/d
	Basal (+FA)	4.3	1.9 kg/d
Lactation	Corn/SBM	1.2	Ad lib
Nursery	Corn/SBM/Whey	2.4	Ad lib
Grower	Corn/SBM	2.0	Ad lib

[a]Folic acid (FA) analyzed via Quantaphase II B_{12}/Folate Radioassay, Bio-Rad.

After 98 days on the basal diet, sows within each littermate pair were synchronized by feeding 14 mg Regumate per day per sow for 14 days and then artificially inseminated with semen from the same boar (high lean growth genotype). Thus, genetic variation in offspring of littermate sows was minimized.

On the day following insemination, sows within each littermate group were randomly allocated to treatment groups (0 or 8 mg supplemented folic acid per day) and feeding of experimental diets (Table 1) was initiated. At 5±2 days post-breeding, ovulation rate was determined via laporatomies and visually counting the number of corpus lutea present on each ovary.

During the gestation period, sows were individually penned in 2 ft X 7 ft stalls on a slotted floor. Sows consumed water ad libitum. Blood samples were collected weekly during the depletion period and from day 28 to 105 of gestation.

On approximately day 109 post-breeding, sows were moved to farrowing rooms. Each pig farrowed was caught prior to nursing the dam, weighed, and numbered via ear notches. Two piglets from each litter were sacrificed via jugular injection followed by intracardial injection of sodium pentobarbital immediately post-weighing. These pigs were exsanguinated and frozen for later dissection and removal of the thymus and spleen. All subsequent pigs born were allowed to nurse immediately following weighing. Colostrum samples were collected after the birth of the first piglet but prior to any piglets nursing. Litters were standardized to 10±2 pigs in an attempt to minimize variability in milk demand among litters.

From approximately day 109 of pregnancy through lactation, sows were housed in individual farrowing stalls on slotted floors. Sows were allowed to consume a fortified, corn-soybean meal diet (1.2 mg of FA/kg diet) ad libitum from parturition through weaning (Table 1).

At 11±2 days of age, two pigs per litter were weaned into a high immune challenge environment consisting of a continuous flow nursery located within the original sow complex. All pigs were individually penned in 1.5 ft X 4 ft pens on slotted floors. All pigs were fed a fortified corn-soybean meal-whey diet formulated to meet or exceeded all NRC recommendation for this age pig (5) (Table 1). Pigs were allowed to consume feed and water ad libitum. Body weights and feed consumption were determined at weekly intervals. Pigs also were bled on day 0 (weaning), 7, 14, and 21 for determination of serum lymphocyte distribution.

At 76±4 days of age, one pig from 12 representative litters per sow treatment were moved into a separate grower room where they were injected intramuscularly with 1 ml of 20% sheep red blood cell (SRBC) on days 0 and 21 of this phase of the study. Blood samples were collected weekly and analyzed for an agglutination response to SRBC.

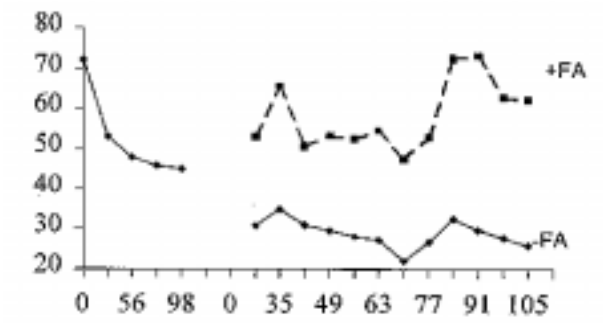
Data were analyzed by analysis of variance techniques using general linear models (GLM) procedures of SAS (6). The sow was considered the experimental unit. Initial primary and initial secondary agglutination response was used as a covariate for the SRBC response data.

Results and Discussion

Gestational FA supplementation increased (P<.05) sow serum folic acid concentration (Figure 1). Folic acid supplementation did not affect the number of pigs per litter (8.37 vs. 8.15) or litter birth weight (10.90 vs. 11.52 kg).

Gestational folic acid supplementation did not alter immunoglobulin (IgG and IgA) concentration in sow serum (gestation day 105), piglet serum, or colostral whey (Table 2). Significant relationships did exist between immunoglobulin concentration in sow serum and colostral whey and between IgA concentrations in sow and pig serum. No relationship existed, nor was one expected, between immunoglobulin concentrations in colostral whey and piglet serum, as the piglets were not allowed to nurse colostrum prior to blood sampling.

Sow Serum Folic Acid Concentrations, ng/ml



Day of Depletion[a] Day of Pregnancy[b,c]

[a]Number of observations=8.
[b]Number of observations=39.
[c]Effect of FA supplementation, P<.05.

Figure 1. Serum folic acid concentration in sows fed the basal diet prior to pregnancy and the basal diet supplemented with 0 (-FA) or 8 (+FA) mg of FA per day during pregnancy.

Table 2. Immunoglobulin (Ig) concentrations (mg/ml) in sow serum (gestation day 105), colostral whey, and piglet serum (presuckle).

		Sow FA Status	
Criteria	Ig	-FA	+FA
Sow serum (d 105)	IgA	22.8	19.9
	IgG	23.9	22.9
Colostral whey	IgA	14.5	15.1
	IgG	31.8	27.6
Pig serum (presuckle)	IgA	0.5	0.6
	IgG	1.8	2.5

Sow serum IgG related to whey IgG, R^2=.38, P<.05.
Sow serum IgA related to whey IgA, R^2=.52, P<.05.
Sow serum IgA related to pig serum IgA, R^2=.19, P<.05.

Gestational folic acid supplementation did not alter thymus or spleen weight, DNA, or protein content of piglets at birth, but resulted in a lower (P<.01) percentage of CD2+ lymphocytes in blood of pigs postweaning. Because the CD2 marker is present on all T cells, this effect would imply that piglets from sows supplemented with folic acid had a lower percentage of circulating T cells during this time. In the SRBC challenge period, folic acid supplementation during gestation did not affect the primary antibody response of piglets. But, gestational folic acid supplementation did increase (P<.05) the offspring's secondary antibody response to a SRBC challenge (Figure 2).

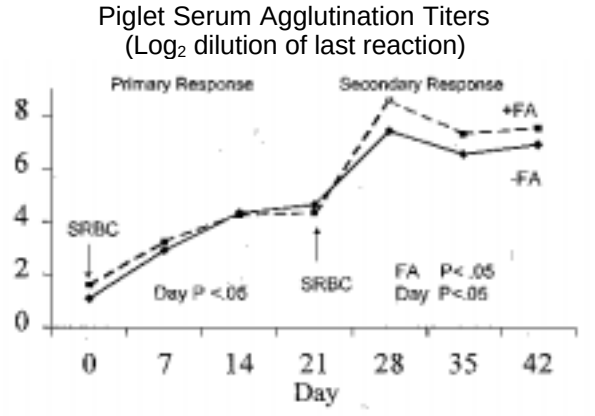


Figure 2. Agglutination response of piglets injected with 1 ml of 20% SRBC on day 0 and day 21.

These results would indicate that the secondary response, which is typically more specific, rapid, and of a greater magnitude, is enhanced by gestational FA supplementation. Based on these data, FA status of the gravid dam influences the dam's serum FA concentrations and postnatal immune response of the offspring.

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