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Dexamethasone Increases *de Novo* Fatty Acid Synthesis in Fetal Rabbit Lung Explants

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ABSTRACT. The effects of dexamethasone on pulmonary *de novo* fatty acid synthesis were investigated in a fetal rabbit lung explant model. Culture of the explants for 2 or 6 days with dexamethasone produced a 48% increase in *de novo* fatty acid synthesis, measured by ^3H_2O incorporation, and a 2.5-fold increase in [^{3}H-methyl] choline incorporation into phosphatidylcholine. A dose-response study showed this effect pleateaued at dexamethasone concentrations above 10^{-9} M. The distribution of the products of *de novo* fatty acid synthesis was altered by dexamethasone. Treated cultures had a 2.5-fold increase in esterification of the newly synthesized fatty acids to phosphatidylcholine and an increase in the proportion of all newly synthesized fatty acids that were used for phosphatidylcholine synthesis. Dexamethasone treatment significantly increased the total fatty acid content and the phosphatidylcholine fatty acid content of the explants by 27 and 85%, respectively. The newly synthesized fatty acids were esterified almost equally to the 1 and 2 positions of phosphatidylcholine; this distribution was not altered by dexamethasone. These studies demonstrate that fatty acid synthesis and distribution are regulated in the fetal lung, at least in part, by glucocorticoids. In addition, coordinate regulation of fetal lung *de novo* fatty acid synthesis and surfactant phosphatidylcholine production by glucocorticoids is likely. (*Pediatr Res* 19: 1272–1277, 1985)

In fetal lung, the rate of surfactant phospholipid synthesis increases dramatically during the last 15% of gestation (1, 2). To synthesize these phospholipids, the lung must have a supply of long-chain saturated fatty acids. The adult lung has several sources of fatty acids for this purpose, including *de novo* fatty acid synthesis within the alveolar type II pneumocyte (3–5), circulating lipids (6, 7), and recycling of endogenous intracellular fatty acids (8). Studies of fetal lung have shown that fatty acids derived from both *de novo* synthesis and exogenous sources can be used for phospholipid synthesis (9–11); the relative importance of these different sources of the fatty acids is not known. With respect to *de novo* fatty acid synthesis in fetal lung, there are parallel increases in the production of disaturated phosphatidylcholine and *de novo* fatty acid synthesis late in gestation (1, 9).

De novo fatty acid synthesis within the fetal lung is an attractive source of phospholipid fatty acids because: 1) circulating lipid levels are low in most mammalian fetuses (12), 2) fetal lungs are relatively less perfused compared to adult lungs (13), and 3) fetal lungs have a large intracellular store of glycogen (1) which may provide energy and substrates for phospholipid biosynthesis (14). In the adult lung, the type II cell is probably the major site of *de novo* fatty acid synthesis (3), suggesting a role for these fatty acids in surfactant phospholipid synthesis. Recent studies show that fatty acids derived from *de novo* synthesis may have a unique role in surfactant synthesis by providing fatty acids for the remodeling of disaturated phosphatidylcholine (6).

Although fatty acids are required for surfactant production and may even participate in the regulation of phosphatidylcholine synthesis (15), very little information is available on the source or regulation of fetal lung fatty acids. Because *de novo* fatty acid synthesis increases sharply in the latter stages of gestation, we studied the regulation of this source in fetal lung. Several studies have shown that glucocorticoids regulate fetal lung disaturated phosphatidylcholine production and glycogen content (16–18). In this study, we investigate the effects of dexamethasone on the rate of *de novo* fatty acid synthesis and the distribution of the newly synthesized fatty acids among lung lipid species in a fetal rabbit lung explant model.

MATERIALS AND METHODS

Fetal lung explants. Organ cultures of lung explants were prepared from fetal rabbits as described by Longmuir *et al.* (19) and modified to be similar to a method used for fetal rat lung (20). Timed pregnant does were killed by intravenous injection of pentobarbital and the fetuses removed under sterile conditions. The lungs were excised and dissected free from nonpulmonary tissue. Explants were prepared by chopping the lungs into 1 mm^3 cubes with a McIlwain tissue chopper. The explants were placed in sterile 60 mm^2 tissue culture dishes on parallel lines scratched into the surface of each dish. The explants were allowed to adhere to the scratched surface for 2 h in 2 ml Waymouths MB 752/1 medium containing 10% fetal calf serum, 100 μg/ml streptomycin, and 100 U/ml penicillin. The fetal calf serum (Hyclone Labs, Logan, UT) was chosen from lots that had low hormone concentrations. The final concentrations of cortisol and T_3 were 20 and 7.2 ng/dl, respectively. For cortisol, this value is 8% of the nuclear binding Kd of this hormone in fetal rabbit lung (21). For T_3, this value is approximately equal to the Kd for this hormone (22). Binding by plasma proteins lowers the free T_3 concentration to a much lower value, however. After 2 h, the cultures were rocked from side to side (three cycles/min) in an environment of humidified 95% O_2–5% CO_2 at 37° C. Cultures were maintained for up to 6 days and the medium was changed daily. Incubations with radiolabeled tracers were for 1–3 h at various times in the culture period. Final specific activities for radioactive precursors were 4.5 nCi/μmol ^3H_2O and 1.12 μCi/μmol [^{3}H-methyl] choline chloride. The final concentration of choline chloride was 1.61 μM.

Lipid extraction and analysis. After incubation, the medium

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was removed and the tissues were washed three times in cold 0.9% NaCl and homogenzied. The lipids were extracted from the homogenate by the method of Bligh and Dyer (23); for studies with ^3H_2O, the chloroform layer was washed once with water. Fatty acids in the total lipid extract were saponified in 10% KOH–50% methanol for 2 h at 85° C (9) and the saponified mixture was washed three times with light petroleum ether to remove unsaponified lipids. The fatty acids were acidified with 3 N H_2SO_4 and extracted in three washes of light petroleum ether. Preliminary studies showed that 90% of phospholipid fatty acids were obtained using this method. The fatty acid fraction was 99% free of the remaining lipid glycerol. The petroleum ether was evaporated under N_2 at 37° C and the radioactivity of the residue determined by liquid scintillation counting in ACS II (Amersham, Arlington, VA) using external standards for quench correction. Radioactivity of the lipid glycerol was determined by counting an aliquot of the remaining aqueous phase of the saponified total lipid mixture.

Phosphatidylcholine and neutral lipids were separated from the total lipid extract by thin layer chromatography on LK-5D plates in a solvent system of chloroform-methanol-7M NH_4OH (65:35:5) v/v). The chromatogram was visualized by exposure to Rhodamine-6G and compared to standards. Disaturated phosphatidylcholine was separated as described by Mason *et al.* (24). Crude phosphatidylcholine was eluted from the gel with two washes of chloroform-methanol–0.001 M acetic acid (20:40:16 v/v) and treated with OsO_4. The disaturated phosphatidylcholine was separated by thin-layer chromatography in a solvent system of chloroform-methanol-7 M NH_4OH (80:28:6 v/v). The spots were visualized with Rhodamine-6G and compared to standards. The fatty acid moieties of phosphatidylcholine, neutral lipids, and disaturated phosphatidylcholine were separated by saponification of these species after they were eluted from the silica gel.

Fatty acids in positions 1 and 2 of phosphatidylcholine were separated by sequential treatment of this phospholipid with phospholipase A_2 and KOH-methanol hydrolysis. After elution the phosphatidylcholine was mixed with phospholipase A_2 (0.8 mg/ml) in 100 mM Tris-HCl (pH 7.5), 10 mM $CaCl_2$ and diethyl ether for 15 min. Preliminary studies demonstrated the reaction was complete within 5 min. The ether phase was evaporated, the solution acidified with 1 N HCl and the liberated fatty acids extracted into petroleum ether. The remaining aqueous phase was subject to hydrolysis in KOH-methanol to remove the fatty acid in position 1, as detailed above.

The fatty acid composition of the total lipid extract was analyzed by gas-liquid chromatography. Methyl esters of fatty acids were prepared by mixing the dried total lipid extract with 2% H_2SO_4 in methanol and heating to 80°C for 1 h. The methyl esters were extracted three times in ethyl ether, which was then washed once with 0.1% $NaHCO_3$ and once with water. Chromatography was accomplished at an oven temperature of 180° C on a 6 foot column packed with 10% SP 2330 on 100/120 chromasorb W AW (Supelco, Bellefonte, PA). Individual fatty acid methyl esters were identified by comparison of retention times to standards.

Enzyme analysis. Lysophosphatidylcholine:acyl-coenzyme A acyltransferase activity was determined by measuring the incorporation of [^{14}C] palmitoyl coenzyme A and [^{3}H] oleoyl coenzyme A into phosphatidylcholine in the presence of the specific acceptor 1-palmitoyl-2 lysophosphatidylcholine. Substrate concentration and buffer composition were as described previously for adult type II pneumocytes (25).

Analytic methods. Fatty acid content was measured by ^{63}Ni binding as described by Ho (26) using palmitate as the standard.

Protein concentration was determined by the method of Lowry *et al.* (27) using bovine albumin as the standard.

Materials. Radiochemicals were obtained from Amersham (Arlington, VA). Dexamethasone phosphate and other biochemicals were purchased from Sigma Co (St. Louis, MO). Culture media was obtained from Gibco (Grand Island, NY).

Statistical methods. Data were analyzed for statistically significant differences by Student's *t* test for unpaired and paired samples.

RESULTS

Fatty acid synthesis. Light microscopy of hematoxylin and eosin stained sections prepared from explants cultured for up to 6 days showed healthy fetal lung tissue (data not shown). To determine the characteristics of *de novo* fatty acid synthesis in the fetal lung explants, ^3H_2O incorporation into total saponifiable fatty acids was measured in explants prepared from 23-day gestation rabbits cultured for 0, 2, and 6 days (Table 1). This gestational age was chosen because it precedes the rapid biochemical maturation of fetal rabbit lung. There was an initial increase in fatty acid synthesis between 0 time and 2 days in culture, followed by no significant change in the rate of ^3H_2O incorporation at 2 and 6 days. Similarly, there were no significant changes in protein content (Table 1), or the rate of lipid glycerol synthesis between 2 and 6 days in culture (Table 2). That protein content does not change during the culture period indicates that the tissues are maintained but not actively growing. Choline incorporation at 0 time (0.23 ± 0.05 nmol/mg/h, $n = 3$) was not statistically different from 2 or 6 days in culture (Table 2). Failure of choline incorporation into phosphatidylcholine to increase in control cultures suggests that an exogenous agent may be necessary to induce maturation in this system. To test the response to glucocorticoids, we measured the effects of dexamethasone on [^{3}H-methyl] choline incorporation into phosphatidylcholine. Two or 6 days exposure to the hormone (1 μM) resulted in a 3-fold stimulation of phosphatidylcholine synthesis (Table 2).

Explant cultures prepared from 23-day gestation rabbits and cultured in dexamethasone (1 μM) for 6 days had a 48% increase in the rate of ^3H_2O incorporation into total saponifiable fatty acids compared to controls (Table 1). Explants cultured in 1% serum had a similar increase in *de novo* fatty acid synthesis with dexamethasone treatment (data not shown) suggesting that 10% serum is not required to achieve this effect. Explant cultures prepared from 20-day gestation animals also responded to dexamethasone with a significant increase in fatty acid synthesis. A

Table 1. *Effects of dexamethasone on fatty acid synthesis in fetal rabbit lung explants**

Tissue source (n)	Days in culture	Protein content (mg/dish)		^3H_2O incorporation into fatty acids (nmol/mg protein/hr)	
		Control	Dexamethasone	Control	Dexamethasone
23 day fetal (4)	0			9.9 ± 2.0	
23 day fetal (10)	2	3.46 ± 0.65	3.13 ± 0.42	24.4 ± 2.0	36.3 ± 3.1†
23 day fetal (9)	6	3.41 ± 0.56	3.42 ± 0.45	24.7 ± 2.0	36.4 ± 1.6‡
20 day fetal (6)	6	2.49 ± 0.35	2.05 ± 0.12	22.4 ± 1.2	35.8 ± 3.1†

* Values are mean ± SEM of (n) experiments performed in triplicate. Explants were prepared from 23 day gestation or 20 day gestation rabbit fetuses and cultured 0, 2, or 6 days without (control) or with 1.0 μM dexamethasone.

† Significantly different from control, $p < 0.005$ by unpaired *t* test.

‡ Significantly different from control, $p < 0.001$ by unpaired *t* test.

Table 2. *Effects of dexamethasone on phosphatidylcholine and lipid glycerol synthesis in fetal rabbit lung explants**

Tissue source	Days in culture	Choline incorporation into phosphatidylcholine (nmol/mg protein/h) (*n*)	Control	Dexamethasone	^3H_2O incorporation into lipid glycerol (nmol/mg protein/h) (*n*)	Control	Dexamethasone
23 day fetal	2	(3)	0.32 ± 0.05	1.01 ± 0.19†	(6)	7.53 ± 1.5	9.10 ± 1.7
23 day fetal	6	(3)	0.29 ± 0.04	0.91 ± 0.04†	(10)	6.95 ± 0.79	8.65 ± 0.92
20 day fetal	6				(3)	9.23 ± 1.9	11.16 ± 2.5

* Values are mean ± SEM. Explants were prepared as outlined in the text and cultured for the indicated period without (control) or with 1.0 μM dexamethasone.

† Significantly different from control, $p < 0.025$ by unpaired *t* test.

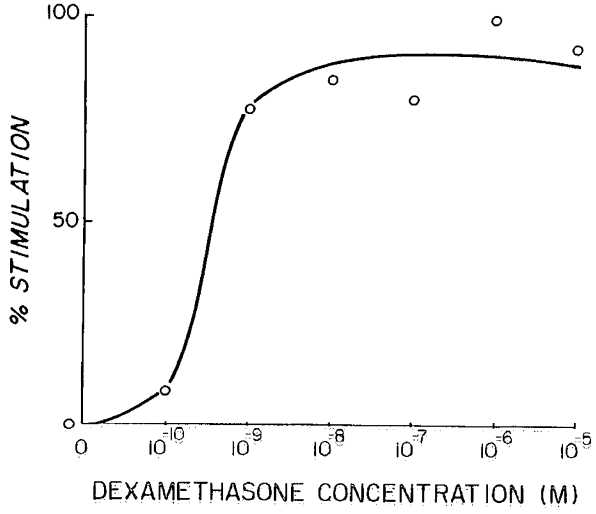

Fig. 1. Effect of varying concentration of dexamethasone in culture medium on ^3H_2O incorporation into total fatty acids by fetal rabbit lung explants in organ cultures. Lung explants were cultured for 6 days in media supplemented with dexamethasone. On day 6 the explants were cultured for 2 h in media containing ^3H_2O (4.5 nCi/μmol) and the fatty acids isolated as outlined in the text. Data are the result of one experiment performed in triplicate.

dose-response study (Fig. 1) showed that the augmented fatty acid synthesis in dexamethasone treated tissue pleateaued at concentrations above 10^{-9} M and was unchanged to 10^{-5} M. Culture in dexamethasone for only 2 days resulted in a stimulation of fatty acid synthesis that was similar to culture for 6 days with the hormone (Table 1). Dexamethasone treatment did not significantly alter the rate of ^3H_2O incorporation into lipid glycerol (Table 2) or the protein content of the explants at 2 or 6 days in culture.

Distribution of labeled fatty acids. The distribution of the radiolabeled newly synthesized fatty acids between phosphatidylcholine and neutral lipids was significantly altered by dexamethasone treatment (Table 3). Compared to controls, explants cultured in dexamethasone for 6 days had a 2.5-fold increase in ^3H_2O incorporation into the fatty acid moiety of phosphatidylcholine. The proportion of total fatty acids synthesized *de novo* that were esterified to phosphatidylcholine increased from 33.5% in control cultures to 57.4% in dexamethasone treated cultures. The increased incorporation into the fatty acid moiety of phosphatidylcholine represented all of the dexamethasone stimulated increase in total fatty acid synthesis. A similar increase in newly synthesized fatty acids in phosphatidylcholine is found after 2 days of dexamethasone treatment although the magnitude of increase was smaller and there was no change in the proportion of the newly synthesized fatty acids found in phosphatidylcholine. Dexamethasone treatment for 6 days also resulted in a significant increase in newly synthesized fatty acids isolated from disaturated phosphatidylcholine compared to controls (7.68 ± 0.85 *versus* 10.76 ± 1.16 nmol H_2O/mg protein/h; $p < 0.01$ paired *t* test).

Long-chain fatty acids can be esterified to the 1 or 2 position of pulmonary phospholipids. To determine if *de novo* synthesis can provide fatty acids for both positions and if dexamethasone affects this distribution, we analyzed incorporation of ^3H_2O into the 1 and 2 positions of phosphatidylcholine (Fig. 2). As seen from this experiment, the fatty acids derived from *de novo* synthesis were distributed almost equally into the 1 and 2 positions of phosphatidylcholine. Dexamethasone treatment resulted in increased incorporation of the radiolabeled fatty acids into both positions approximately equally. Saturated fatty acids are the major species labeled by ^3H incorporated from ^3H_2O (28). Saturated fatty acids may be esterified to position 2 through the synthesis of disaturated diglyceride or by remodeling of position 2 of monosaturated phosphatidylcholine. To determine if the dexamethasone mediated increase in incorporation of newly synthesized fatty acids into position 2 may involve increased activity of the remodeling pathway, we determined the activity of microsomal lysophosphatidylcholine:acyl-CoA acyltransferase in treated and control tissues. Dexamethasone treatment resulted in a significant increase in palmitate specific enzyme activity (65.6 ± 9.2 *versus* 84.7 ± 10.0 nmol/min/mg protein; $p < 0.05$, paired *t* test). Activity in the presence of oleoyl-CoA was 6.5-fold lower and was not significantly increased by dexamethasone. This pattern is similar to that reported by Tsao and Zachman (29). Taken together, these data show that 1) *de novo* fatty acid synthesis is a source of saturated fatty acids for disaturated phosphatidylcholine; 2) dexamethasone-stimulated fatty acid synthesis results in increased utilization of these fatty acids for both the 1 and 2 positions of phosphatidylcholine; and 3) dexamethasone treatment increases activity of an enzyme involved in fatty acid remodeling of phosphatidylcholine.

Fatty acid composition and content. The fatty acid composition, determined by gas-liquid chromatography, of a total fatty acid extract of the explants is shown in Table 4. In general, long chain saturated fatty acids are the predominate species. Palmitic acid is the major fatty acid in both the treated and control cultures. Dexamethasone treatment resulted in a small increase in the proportion of palmitic acid, but this finding is not statistically significant. Total fatty acid content of the explants increased significantly by 27% in treated cultures (Table 4). The calculated palmitate content of the tissues increased by 49%. Fatty acid content of phosphatidylcholine increased by 85% while neutral lipid fatty acid content was unchanged (data not shown). These data demonstrate that the augmented synthesis of fatty acids due to dexamethasone noted above is accompanied by increased fatty acid content, especially in the phosphatidylcholine fraction.

DISCUSSION

This study demonstrates that glucocorticoids, which are known to augment surfactant phospholipid synthesis and decrease glycogen content in fetal lung, also increased *de novo* fatty acid synthesis and content in this tissue. In addition, dexamethasone treatment altered the distribution of the newly synthesized fatty acids to favor incorporation into phosphatidylcholine. This resulted in an increased content of phosphatidylcholine fatty acids.

Table 3. *Effects of dexamethasone on distribution of newly synthesized fatty acids**

Culture condition	(*n*)	Days in culture	Neutral lipid fatty acids	(%)	Phosphatidylcholine fatty acids	(%)
Control	(3)	6	3.93 ± 0.88	(15.9)	8.28 ± 1.12	(33.5)
Dexamethasone	(3)	6	6.20 ± 0.55	(17.0)	20.90 ± 1.58†	(57.4)
Control	(3)	2	4.00 ± 0.34	(16.2)	9.93 ± 2.14	(40.6)
Dexamethasone	(3)	2	3.95 ± 0.45	(10.8)	14.83 ± 3.0‡	(40.7)

* Values are mean ± SEM of three experiments performed in triplicate. Explants were cultured with or without 1 μM dexamethasone for the entire culture period. Data are expressed as nmoles H_2O/mg protein/h. Number in parentheses is percentage of total incorporation given in Table 1.

† Significantly different from controls, $p < 0.001$ by paired t test.

‡ Significantly different from controls, $p < 0.05$ by paired t test.

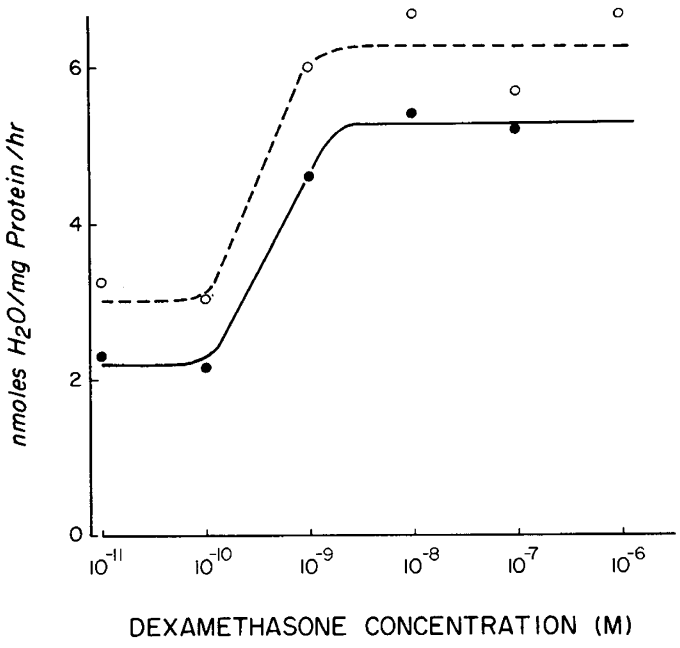

Fig. 2. Effects of dexamethasone on ^3H_2O incorporation into fatty acids of position 1 (*open circle*) and position 2 (*closed circle*) of phosphatidylcholine. This experiment was conducted as outlined in Figure 1. Position 2 fatty acids were removed by treatment of phosphatidylcholine with phospholipase A_2 as outlined in the text. Position 1 fatty acids were hydrolized and saponified from the resultant lyso PC as outlined in the text.

The glucocorticoid stimulation of fatty acid synthesis demonstrated in this study, contrasts with another study that suggested glucocorticoid inhibition of *de novo* fatty acid synthesis in fetal lung (30). This early investigation measured activity of the enzymes of fatty acid synthesis in fetal lungs after maternal glucocorticoid injection and noted decreased activity in fetuses of treated animals. It is known that the activity of these enzymes is strongly affected by circulating hormones and intracellular metabolites (9, 31, 32). Thus, the inhibitory effect of glucocorticoid may have been secondary to alterations in maternal, placental, or nonpulmonary fetal metabolism. In the present study, the explant model allowed direct exposure of fetal lung to the hormone and avoided these confounding variables. The dose range of dexamethasone required to stimulate fatty acid synthesis reported herein corresponds to the Kd of nuclear binding of this hormone in fetal rabbit lung and is similar to that reported for stimulation of phosphatidylcholine synthesis in fetal rabbit lung explants (21).

Because the lung explant model consists of several cell types, it is not possible from this study to identify which fetal cell is the target for dexamethasone stimulation of *de novo* fatty acid synthesis. In the differentiated lung, the alveolar type II cell is probably the major site of *de novo* fatty acid synthesis (9). In the fetal lung, pretype II cells contain large quantities of glycogen that are depleted by glucocorticoid treatment (16) and may provide carbon precursors for disaturated phosphatidylcholine synthesis (14).

Tritium from ^3H_2O is incorporated into fatty acids during the terminal reductive steps in the biosynthesis of fatty acids. The major fatty acid products labeled with ^3H are saturated fatty acids (28). This may occur during microsomal or mitochondrial chain elongation as well as *de novo* fatty acid synthesis. In fetal rabbit lung, however, fatty acid chain elongation is not a major route of long-chain fatty acid synthesis (33). In the present study the increase in the calculated palmitate content accounted for 65% of the increase in total fatty acids.

The ratio of ^3H incorporated into fatty acids from ^3H_2O to carbon atoms used for fatty acid synthesis (^3H:C) has been determined (28). Use of ^3H_2O incorporation, therefore, allows quantitative estimates of the total amount of fatty acid synthesized during the incubation (assuming that the average fatty acid produced is 16:0). Applying these calculations to our data and assuming that there is no recycling of ^3H or [^3H-methyl] choline radiolabels during the short incubations, it is apparent that *de novo* fatty acid synthesis in the control tissue can supply sufficient fatty acids (3.58 nmol/mg protein/h) for all the phosphatidylcholine produced. The additional fatty acids provided after dexamethasone stimulation of the tissue (1.69 nmol fatty acid/mg protein/h) can provide the increased quantity of fatty acids that are required for the dexamethasone augmented rate of phosphatidylcholine synthesis (1.24 nmol fatty acid/mg protein/h). Thus, under these culture conditions, *de novo* fatty acid synthesis is sufficiently active to provide all the fatty acids for phosphatidylcholine synthesis. Use of ^3H_2O incorporation as a measure of *de novo* fatty acid synthesis avoids the confounding effects of intracellular carbon pools that make interpretation of ^{14}C-tracer studies difficult. For example, dexamethasone decreases fetal lung glycogen content; this may result in intracellular dilution of exogenous ^{14}C-labeled precursors used to measure fatty acid synthesis. This process may account for a dexamethasone-mediated decrease in acetate incorporation into phosphatidylcholine noted by another investigator (34).

Fatty acid synthesis and phosphatidylcholine production in fetal lung increase in parallel toward the end of gestation (9). Dexamethasone stimulates both processes. These data suggest that phosphatidylcholine and fatty acid synthesis in fetal lung may be regulated coordinately. Despite extensive studies, the mechanisms of action of dexamethasone on lung phosphatidylcholine synthesis are obscure. Recent data suggest that intracellular free fatty acids may regulate phosphatidylcholine synthesis in lung and liver, implying that increased intracellular fatty acids, at some point, stimulate phosphatidylcholine synthesis. For example, cellular fatty acids promote the translocation of cholinephosphate cytidylyltransferase, which regulates a key step in phosphatidylcholine synthesis, to its active high molecular weight membrane bound form (15, 35). In reference to the present

Table 4. *Effects of dexamethasone on fatty acid composition and content of fetal rabbit lung explants**

Culture condition (n)	Fatty acid species (expressed as % of total)						
	14:0	16:0	16:1	18:0	18:1	18:2	20:4
Control (4)	13.6 ±2.4	35.3 ±1.3	9.2 ±1.2	6.8 ±0.6	12.2 ±2.1	7.8 ±2.1	11.1 ±1.7
Dexamethasone (3)	7.0 ±1.7	41.7 ±5.5	9.9 ±5.7	4.9 ±0.7	12.9 ±2.6	6.7 ±1.7	8.3 ±0.8

	Total fatty acid content (nmol/mg protein)	Calculated palmitate content† (nmol/mg protein)	PC fatty acid content (nmol/mg protein)
Control (7)	1066 ± 162	376 ± 57	(3) 436 ± 110
Dexamethasone (7)	1350 ± 210‡	562 ± 87§	(3) 808 ± 34‡

* Values are mean ± SEM. Explants were cultured as outlined in text for 6 days without (control) or with 1.0 μM dexamethasone.

† Palmitate content is calculated from fatty acid composition and content data.

‡ Significantly different from control, $p < 0.05$ by paired t test.

§ Significantly different from control, $p < 0.01$ by paired t test.

study, stimulation of fatty acid synthesis by dexamethasone may help augment phosphatidylcholine synthesis by increasing cellular fatty acids. Alternatively, augmented production of phosphatidylcholine by dexamethasone may stimulate *de novo* fatty acid synthesis by consuming cellular long-chain acyl-CoAs that inhibit acetyl-CoA carboxylase, a rate-regulating enzyme of *de novo* fatty acid synthesis. The interaction of these pathways to increased surfactant synthesis remains speculative.

In perfused adult lung, the major portion of palmitate synthesized within lung and incorporated into disaturated phosphatidylcholine is found in the 2 position of this molecule, while exogenous palmitate was incorporated preferentially into the 1 position (6). In the present study, fatty acids synthesized *de novo* were incorporated into the 1 and 2 positions approximately equally in both control and dexamethasone cultures. The mechanism of increased esterification to position 2 of phosphatidylcholine induced by dexamethasone may be increased activity of lysophosphatidylcholine acyl-CoA acyltransferase. This enzyme has high activity in adult type II cells (25) and is highly specific for the utilization of palmitoyl-CoA. Although these data imply a dexamethasone effect on the remodeling pathway, we cannot obtain accurate information on the biologic importance of this pathway from the present data. The length of time required for ^3H_2O incubations precluded identification of instantaneous rates of incorporation into positions 1 and 2 of phosphatidylcholine.

In fetal lung, fatty acids derived from both exogenous sources and from *de novo* synthesis can be incorporated into phospholipid fatty acids. The relative contributions of these sources of fatty acids to fetal lung surfactant production are not known. In newborn rabbits, fatty acids synthesized within lung may be used preferentially for surfactant production over exogenous fatty acids (36). This study demonstrates that dexamethasone, which augments fetal lung maturity, increases *de novo* synthesis and alters the distribution of newly synthesized fatty acids to favor inclusion in surfactant phospholipids.

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glucagon in acute hormonal control of hepatic lipogenesis. Diabetes 28:828–835
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Announcements

American Pediatric Society and Society for Pediatric Research Schedule of Annual Meetings

1986—Washington, D.C.—May 5–9

1987—Anaheim, CA—April 27–May 1

1988—Washington, D.C.—May 2–6

1989—Washington, D.C.—May 1–5

1986 Abstract Receipt Deadline: December 2, 1985.

For meeting registration or abstract information, contact: Audrey Brown, M.D., Secretary-Treasurer, American Pediatric Society, Downstate Medical Center, Department of Pediatrics, 450 Clarkson Avenue, Box 49, Brooklyn, NY 11203 (718) 270–1692 or William Berman, Jr., M.D., Secretary-Treasurer, Society for Pediatric Research, Department of Pediatrics, University of New Mexico School of Medicine, Albuquerque, NM 87131 (505) 277–6628.

4th INTERNATIONAL CHILD NEUROLOGY CONGRESS of the International Child Neurology Association (ICNA) Jerusalem, Israel, March 16–20, 1986

Main Topics: 1. Genetic and Environmental Pediatric Encephalopathies. 2. Epilepsy and the Developing Brain. 3. Pediatric Neurologic Diseases with Ultrastructural Pathology. 4. Assessment and Remediation of Young Children with Central Nervous System Dysfunction.

Satellite Symposium: Child Neurology and Developmental Pediatrics (Sharing Issues of Mutual Concern) March 21, 1986.

For further information: Shaul Harel, M.D., ICNA-4 Congress, P.O. Box 29313, Tel Aviv 61292, Israel, Tel: (03) 654541 Telex: 033-554.

In the USA: Tzell Tours, 45 West 34th Street, New York, NY 10001 Tel: (212) 279–3700 Telex: (23) 238426.

26th Meeting of the Teratology Society

The 26th meeting of The Teratology Society will be held from July 7–10, 1986 at the Park Plaza Hotel, Boston, MA 02117. The Behavioral Teratology Society will meet in conjunction with The Teratology Society.

Abstracts must be postmarked no later than February 1, 1986. *For further information please contact the* President of the Society: Dr. Lewis B. Holmes, Embryology-Teratology Unit, Children's Service, Massachusetts General Hospital, Boston, MA 02114, (617) 726–1742.

1986 Written Examination of The American Board of Pediatrics

The 1986 Written Examination of the American Board of Pediatrics will be administered on *Friday, September 12* in various cities throughout the United States, Canada, and Puerto Rico.

Application material for the certifying examinations of the Board is available throughout the year by writing to the Board Office at the address below. The completed material of those applicants who wish to be considered for the 1986 Written Examination must be postmarked by *January 31, 1986.*

Contact: American Board of Pediatrics, 111 Silver Cedar Court, Chapel Hill, NC 27514, 919/929-0461.