tion between 24-hour urinary sodium excretion and blood pressure as measured the same day in black children in the high blood pressure strata (*17*). Gleibermann (*18*) surveyed literature on the relationship between sodium intake and blood pressure in black communities and found a positive association in a composite scattergram. Helmer (*19*) and Gleibermann (*18*) have proposed an adaptive survival advantage for the genetic trait that would have conserved body sodium in blacks by preventing hyponatremic collapse. Sodium losses could have occurred through perspiration and laboring in the heat on a low-sodium diet. The possibility of an increased sodium sensitivity in the upper percentiles of blood pressure for black children deserves consideration in any effort to prevent hypertension.

Horwitz *et al.* (*20*) reported lower D$\beta$H levels in blacks than in whites among 90 normotensive and 70 hypertensive adult subjects, the largest difference occurring among hypertensive subjects. The absence of high-renin–high-D$\beta$H values (*21*) among the black children in the high blood pressure strata of our study clearly points to a racial difference in the hormonal makeup of the candidates for essential hypertension. Sympathomimetic influences on blood pressure and heart rate may be greater in whites and play a greater role in mediating early hypertension.

The present studies are being conducted on asymptomatic children leading normal lives where criteria for hypertension are indefinite. Although the data reported here pertain to children whose selection was based on their blood pressure level at one particular time, an increasing body of statistical evidence now suggests that the children in the high strata tend to remain there throughout childhood and perhaps into adulthood.

In view of our findings, which suggest racial differences in sympathomimetic and hormonal influences on blood pressure levels, approaches to prevention and possibly treatment of early essential hypertension in the two races may differ.

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## Lung Maturation in the Fetal Rat: Acceleration by Injection of Fibroblast-Pneumonocyte Factor

Abstract. *Fibroblast-pneumonocyte factor, produced by the fetal lung fibroblast in response to glucocorticoids, was partially purified by column chromatography on Sephadex G-75. The resulting preparation showed two major and two minor bands on sodium dodecylsulfate–polyacrylamide gel electrophoresis. When fetal rats were injected on day 17 of gestation with 1 microgram of this material, they showed on day 20 biochemical evidence of accelerated lung maturation as compared to littermate controls. There were no differences between the two groups in body weights, organ weights, or circulating corticosteroid levels.*

Preparation of the fetal lung for breathing air depends upon synthesis and secretion of the pulmonary surfactant, which lowers alveolar surface tension with the onset of gaseous ventilation and stabilizes the terminal respiratory units. Surfactant, a complex lipoprotein, is produced by the alveolar type II pneumonocyte whose function is physiologically regulated by glucocorticoid hormones (*1*); it can be precociously induced by administration of exogenous glucocorticoids (*2*).

We have recently shown (*3*) that, although alveolar type II pneumonocytes can be stimulated to produce surfactant by glucocorticoids in mixed primary cell cultures (which contain endothelial, mesenchymal, and epithelial elements), pure cultures of human fetal alveolar type II pneumonocytes show only a minimal response (*4*). This observation ap-

Table 1. Effect of fibroblast-pneumonocyte factor on fetal pulmonary phospholipid profile. Control and experimental left fetal lungs were pooled within each litter ($N = 9$). The extracted phospholipids were separated by two-dimensional thin-layer chromatography (*9*) and quantitated by phosphorus assay (*6*). Results are expressed as the percentage of total phospholipids ± standard deviation.

| Phospholipid | Control | Experimental |
|---|---|---|
| Phosphatidylcholine | 42.6 ± 2.3 | 49.2 ± 2.5* |
| Disaturated phosphatidylcholine† | (25.7 ± 1.6) | (40.9 ± 2.9)* |
| Phosphatidylglycerol | 0.5 ± 0.2 | 1.1 ± 0.2* |
| Lysophosphatidylcholine | 5.7 ± 0.2 | 5.4 ± 0.2 |
| Lyso-*bis*-phosphatidic acid | 7.8 ± 1.4 | 7.4 ± 2.0 |
| Phosphatidylinositol | 5.8 ± 0.8 | 6.4 ± 1.2 |
| Phosphatidylethanolamine | 20.1 ± 3.1 | 18.9 ± 2.6 |
| Phosphatidylserine | 8.0 ± 1.9 | 5.3 ± 1.5 |
| Total | 90.5 ± 1.9 | 93.7 ± 2.8 |

*$P < .001$ †Percentage of phosphatidylcholine fraction found to be disaturated, as determined by the osmium tetroxide technique (*6*).


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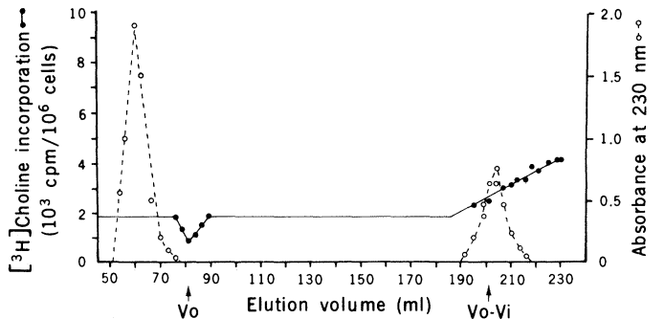


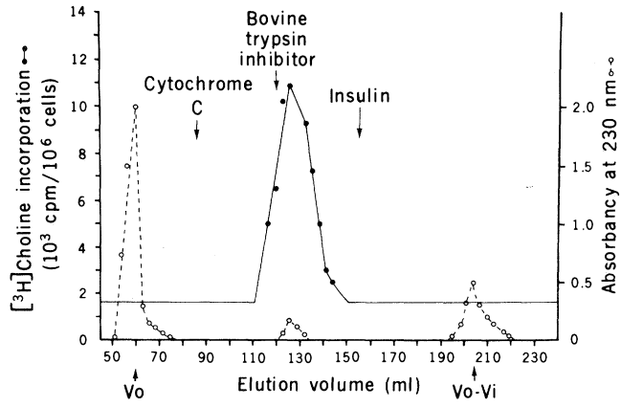


Fig. 1. Sephadex G-75 chromatography of fibroblast-pneumonocyte factor. Lyophilized, desalted medium (100 ml) collected from cortisol-treated fetal lung fibroblasts was applied to a 2.5 × 60 cm column of Sephadex G-75 and eluted with 0.02*N* HCl. Three ml fractions were collected and analyzed for protein content (absorbance at 230 nm, dotted line) and for their effect on [$^3$H]choline incorporation into disaturated phosphatidylcholine (DSPC) by human fetal alveolar type II cell cultures (solid line; see text). A small inhibitory peak is evident at the elution volume of 80 ml, while stimulatory activity appears to be largely retained on the column. Fig. 2. Sephadex G-75 chromatography of fibroblast-pneumonocyte factor. The experimental design was the same as in Fig. 1, except that the column was equilibrated and run with 1*M* acetic acid. Arrows represent elution volumes of three marker proteins (cytochrome C, 12,300 daltons; bovine trypsin inhibitor, 6160 daltons; insulin, 5200 daltons). As shown, inhibitory activity is not detected under these conditions, but stimulatory activity (fibroblast-pneumonocyte factor) elutes as a single peak with apparent molecular weight of between 5000 and 7000.

pears to be related to steroid-induced production by the fetal lung fibroblast of a heat-stable, dialyzable polypeptide, fibroblast-pneumonocyte factor, which in turn induces biochemical activity in the alveolar type II pneumonocyte (*4*). In this report, the experiments were designed to determine whether a partially purified preparation of fibroblast-pneumonocyte factor possessed the ability to accelerate lung maturation in vivo.

I desalted 100 ml of lyophilized serum-free minimum essential medium containing $10^{-6}M$ cortisol; the medium had been recovered after 24 hours incubation (10 ml per 75 cm$^2$ of cells) with confluent cultures of human fetal lung fibroblasts (*4*) and desalted by Sephadex G-10 chromatography. The desalted material was lyophilized, dissolved in 1*M* acetic acid, and chromatographed on a calibrated column (2.5 × 60 cm) of Sephadex G-75 in 1*M* acetic acid (Figs. 1 and 2). Fractions of 3 ml were collected in siliconized tubes, and the type II pneumonocyte-stimulating activity (fibroblast-pneumonocyte factor) was recovered as a single peak in the apparent molecular weight range between 5 and 7 × $10^3$. I lyophilized the combined active fractions and dissolved the residue in 5 ml of 2 *N* HCl which was then neutralized with 5 ml of 2*N* NaOH (*5*).

This preparation (0.01 ml containing 1 μg of protein) was injected intraperitoneally into fetal rats on day 17 of gestation (term = 22 days) (*6*). Control fetuses in the contralateral uterine horn received 0.01 ml of 1*N* NaCl. A total of nine litters, which included 32 experimental fetuses and 35 control fetuses, were studied.

Early on day 20 of gestation, the mother rats were killed and the fetuses were removed to study body and organ weights, corticosteroid levels, and biochemical indices of lung maturity. I observed no significant difference ($P > .05$, Student's $t$ test) in: (experimental versus control, means ± standard deviation) body weight (2.4 ± 0.5 versus 2.4 ± 0.4 g); lung weight (89.5 ± 11.0 versus 93.7 ± 13.1 mg); adrenal weight (1.9 ± 0.5 versus 2.4 ± 0.8 mg); or circulating corticosterone levels (*6*) (41.8 ± 8.5 versus 48.4 ± 7.4 ng/ml).

The right lung of each fetus was homogenized and incubated in 2 ml of minimum essential medium containing [$CH_3$-$^3$H]choline chloride (New England Nuclear, specific activity 84 Ci/mmole). The incubation was carried out at 37°C under an atmosphere of 5 percent $CO_2$ in air for 2 hours. The lipids were extracted, and disaturated phosphatidylcholine was isolated (*6*). The incorporation of tritium into disaturated phosphatidylcholine (the major functional component of the pulmonary surfactant) was increased in fibroblast-pneumonocyte factor injected fetuses to 1418 ± 189 dis/min per milligram of tissue per hour compared to 909 ± 123 in the controls ($P < .001$). Pulmonary phospholipid profiles, determined on the pooled experimental and control left lungs of each litter (Table 1) reveal a relatively specific effect on the pulmonary content of the surfactant-associated phospholipids, disaturated phosphatidylcholine, and phosphatidylglycerol.

I conclude that the fetal lung fibroblast, in response to glucocorticoids, produces a polypeptide factor (or factors), which stimulates the biochemical activity of the alveolar type II pneumonocyte and accelerates fetal lung maturation in vivo. Of particular note is the observation that, unlike steroid-accelerated lung maturation which is associated with a reduction in pulmonary cellular growth (*3, 6, 7*), the acceleration of fetal lung maturation with fibroblast-pneumonocyte factor is unassociated with major changes in lung weight. Epithelial-mesenchymal interactions, long appreciated as critical in early embryonic organogenesis (*8*), may have a hitherto unappreciated function in promoting the expression of mature epithelial cellular behavior.

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