The biosynthesis of phosphatidylcholine molecular species in fetal and neonatal guinea pig lung.

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Lung collapse upon expiration is prevented by the surface tension properties of pulmonary surfactant [1]. The effectiveness of surfactant in preventing alveolar collapse is dependent upon the phosphatidylcholine (PC) molecular species composition. The surfactant of premature infants contains reduced amounts of PC16:0/16:0 and is inefficient at preventing alveolar collapse resulting in acute respiratory distress syndrome (RDS) [2]. Towards term the amount of PC16:0/16:0 increases. Therefore the ability to produce functional surfactant is dependent upon gestational age.

The guinea pig has been proposed as a model for human infants [3]. Pups delivered preterm show survival rates and pathological changes comparable to those found in premature human infants. In order to investigate the changes in lung PC composition and biosynthesis which occur in the later stages of guinea pig lung development pups were injected i.p. in utero with 50µCi [14C]-choline. Comparison of the total PC composition with that synthesized de novo allowed the degree of remodelling of newly synthesized phospholipid to be assessed. After 3 hours pups were delivered by Caesarian section, the lungs blanched and lavaged, and processed for PC analysis or preparation of microsomes and lamellar bodies. Analysis of the PC molecular species composition in each fraction was carried out by fluorescence HPLC [4]. [14C]-choline labeled PC was measured by HPLC with radiochemical detection [5].

At all three gestational ages studied the tissue PC composition closely reflected that of the microsomal fraction. Between d55 and d68 the tissue and microsomal concentrations of disaturated PC increased. PC16:0/16:0 increased from 27% to 32% (d65) and 40% at term (d68). Also, PC14:0/16:0 increased from 7.5% to 13.8%. During this period the percentage concentration of PC16:0/18:1 decreased from 32% to 19%. However, the amount of PC16:0/16:0 at term decreased significantly. d55 guinea pig lungs do not secrete surfactant or contain appreciable amounts of lamellar bodies [6]. The lamellar body fraction showed an increase in PC16:0/16:0 between d65 and d68 of 13%. Concomitant with this the amount of 16:0/16:1 and 16:0/18:2 decreased by 7% and 3% respectively. The lavaged surfactant was slightly enriched in saturated PC (32%) between d65 and d68 and showed a slight decrease in PC16:0/16:2. The composition of the surfactant fraction at both d65 and d68 was found to contain less PC16:0/16:0 and PC16:0/18:1 and more PC16:0/18:2. This may suggest conversion of the saturated species to the disaturated species via a phospholipase A2 dependent acyl remodelling mechanism. Between d55 and d68 the ratio of de novo synthesized to total tissue PC for each molecular species did not change significantly, with the exception of PC16:0/18:1 which showed increased synthesis during this period. This indicated that the remodelling processes which operate on the de novo pool were active at all gestational ages irrespective of the degree of lung maturity. Therefore, the differences in total tissue composition between d55 and d68 may be attributed to changes in the composition of substrate diacylglycerol and acyl-CoA rather than to changes in enzyme specificity for the remodelling processes. The degree of enrichment of unsaturated PC in the lamellar body and surfactant fractions between d65 and d68 correlates with previous survival data for animals of these gestational ages [3]. Since the remodelling systems appeared to be functional at the earliest gestational age investigated, the limiting factor for the synthesis of PC with a molecular species composition characteristic of functional surfactant would seem to be the availability of remodelling substrates. These results emphasise the importance of acyl-CoA composition and concentration on the specificity of lung PC synthesis.

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