Postnatal Lung Development and Its Important by Glucocorticoids

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In human lung development we distinguish a pre- and a postnatal period. After the formation of the lung diverticulum from the foregut at gestation day 26, the further development can be subdivided into 5 stages [1]. In the pseiidoglandular stage (prenatal weeks 5-17) the lung bud grows and divides dichotomously several times into a loose meshwork of mesenchyme giving the organ a gland-like appearance. During the next stage {canalicular stage, weeks 17-24) the future lung parenchyma is 'canalized' by numerous capillaries. Epithelial differentiation is started, so that type-I pneumocytes contribute to a thin air-blood barrier and type-II pneumocytes begin to secrete surfactant into the liquid-filled air spaces. In the following saccular stage (24 weeks to birth) the future gas-exchange region expands, the interstitial tissue in between the air spaces decreases giving the lung a more aerated appearance. The stage alveolization starts a few weeks before birth and lasts beyond it. The air spaces of the saccular stage are now being subdivided by new septa, thus forming the alveoli. Postnatally the alveolar formation continues until about the 2nd year,

but the 'bulk alveolar formation, is likely to be completed until about the 6th month of age [2]. During alveolization the saccular walls and also the new septa consists of a broad central sheet of connective tissue with a capillary layer on each side. In our opinion this double capillary layer is a prerequisite for alveolar formation as the newly formed septa arise by upfolding of one of the two layers. By this process, the prospective parenchymal air spaces turn into alveolar ducts and sacs lined by the future alveoli. In the last stage of lung development the bilayered 'primitive, septa turn into the slender mature interalveolar walls of the adult lung containing only a single capillary layer. This period of microvascular maturation begins shortly after birth in parallel to the alveolization. It is characterized by a pronounced decrease in interstitial tissue mass leading to the approximation of the two capillary layers which come into close contact and merge [3].

The Influence of Glucocorticoids

Glucocorticoids (GCs) are well known as a major therapeutic agent in preterm neonates with respiratory problems. They were initially found prenatally to accelerate the maturation

thinning of the inter air space walls. Weeks following the drug administration, the air spaces of adult rats remained enlarged compared to those of control animals. Based on our concept that alveolization is only possible in a lung parenchyma of primitive structure (walls with double capillary networks), we hypothesized that GCs might be untimely in accelerating the septal maturation before alveolization had time to occur to a large extent. We therefore investigated the qualitative and quantitative changes in the rat lung structure under GC treatment by means of light and electron microscopic morphometric techniques [5]. We administered a low dose of 0.1 µg dexamethasone-phosphate daily during 2 weeks (postnatal days 2-15) and studied the lungs from days 4-60. The GCs did not influence body weight gain or lung volume considerably during the observation period. However, during the first 13 days, GC treatment substantially enhanced alveolar wall thinning and also reduced the absolute volume of septal tissue, particularly of the interstitial component. Micro vascular maturation was accelerated (more numerous septa with a single layer of capillaries than in controls) and the number of new septa was clearly decreased. One week after withdrawal of GC treatment, the precocious maturation seemed to be reversed. Now the GC animals showed thicker septa, reappearance of a double capillary layer and new septal crests, all this indicating a kind of catch-up process. Despite this attempt of recovery, the sequelae of GC administration were a rather 'emphysematous' looking lung with larger and fewer air spaces. The mean linear intercept (an estimate for the alveolar diameter) was increased and the surface of the air/tissue interface decreased in treated animals compared to controls ($p < 0.1$).

In conclusion GC treatment prevented the formation of the full complement of alveoli despite the additional 'second-round' alveolization.

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Extended Abstracts

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