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Morphological Development of the Human Fetal Lung

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= Abstract =The morphological development of the human fetal lung was studied analysing a total of 198 human fetal lungs, including lungs of 16 embryos.

The weight of the lung increased progressively from 0.7 gm at 9-12 weeks of gestation to 45.2 gm at 37-40 weeks, and the right lung constituted 54 % of total lung weight. The lung, fixed in the inflated state with negative pressure of 24-25 cm H_2O, increased rapidly in its volume at 24-25 weeks of gestation, coinciding with the development of saccules. Reconstruction of the embryonal lungs revealed the presence of lung buds at 4 weeks, stem bronchi at 5 weeks, segmental bronchi at 6 weeks, and subsegmental bronchi thereafter.

Histological characteristics were analysed with special emphasis on sequential development of the functioning respiratory units. The period of 4-8 weeks was characterized by budding of large bronchi and appearance of pleura and lobar pattern. During the period of 9-16 weeks, conducting airways were laid down associated with development of cilia and mucous glands. At the period of 17-28 weeks acinar canals were proliferating and were followed by flattening of epithelium and vascularization. Well developed saccules appeared by the end of this period. During the period of 29-36 weeks, progressive thinning of septa was noted, accompanied by segmentation of saccules by developing secondary crests. As a result well developed alveoli with delicate septum and a single capillary system could be identified at the period of 37-40 weeks.

The height of the epithelium at the terminal buds showed gradual decrease from 36 μm at 5 weeks to 5.8 μm at 21 weeks of gestation.

Key Words : ***Fetus, Lung, Embryology***

INTRODUCTION

The study of the development of the lung through which will be gained the insight into the pathogenesis and sequelae of congenital malformations, is of utmost importance as the presence of a mature pulmonary system is critical to the survival of premature infants.

The lung appears as an outpouching from the esophagus during the early embryonic period, then undergoes marked structural changes during prenatal development, and is thereby transformed into a highly vascular organ. The lung growth in utero can be arbitrarily divided into 5 stages; embryonic, pseudoglandular, canalicular, saccular, and alveolar peiod (Langston *et al.* 1984). In the embryonic period starting from conception to 5 weeks of gestation, the lung buds, the main and lobar bronchi are formed. During the pseudoglandular period, from 6 to 17 weeks, bronchial branching is completed. From 17 to 24 weeks (Hislop and Reid 1974) or 28 weeks (Langston *et al.* 1984) comprising the canalicular period, the pulmonary lobules are formed and vascularized, and acini are subsequently formed. During the saccular period, from the end of the canalicular period to 36 weeks, the respiratory bronchioles and saccules are formed. Although small laboratory animals are born with the lungs in the saccular stage (Amy *et al.* 1977), a phase of in-utero alveolar development, the alveolar period, has been identified in the human (Loosli and Potter 1959; Emery and Mithal 1960; Langston *et al.* 1984).

Although the structural development of the lung has been well studied in a variety of laboratory animals (Boyden 1961; Burri *et al.* 1974; Burri 1974; Amy *et al.* 1977), only a few human infants and fetuses have been studied, and there is still fewer available quantitative data (Emery and Mithal 1960; Dunnil 1962; Davies and Reid 1970; Thurlbeck and Angus 1975).

The above mentioned developmental stages are a continuous event, and many studies have been limited to describing only a part or parts of the stage. In Korea, the only available studies on the human lung development are limited to those of Yang (1965) and Chung (1966), which were focused on just the external measurements of the fetal lung.

In view of these reasons, the authors undertook this study in the hope of broadening the spectrum of histogenetic data necessary for understanding the growth of the human fetal lung, concentrating primarily on observing the change in lung weight, volume, and the branching patterns of the embryonal bronchus.

MATERIALS AND METHODS

A total of 198 fetal lungs including 16 embryonal ones were analysed. These were the products of artificial or spontaneous abortion, or of infants who died soon after birth. Those from multiple pregnancy, with congenital anomalies on gross examination, or showing infection on microscopic examination were excluded from the study.

Sixteen embryos and eleven fetuses of 9~10 weeks of gestation were fixed in 10 % formalin and embedded in paraffin *en bloc* after measuring crown-rump(CR) length and body weight. Serial sections of the specimens were observed and the branching pattern of the bronchi of 12 embryos was reconstructed. In the fetuses over 11 weeks of gestational age, the body weight, CR length, the weight of major organs (the lung, kidney, spleen, heart, adrenal gland, and thymus) were measured during full autopsy. The lung blocks obtained mainly from the central part of the upper lobe were fixed in formalin and embedded in paraffin.

The lungs of 37 fetuses were inflated with a negative pressure of 24~25 cm H_2O and fixed with formalin vapour using the apparatus illustrated in Fig. 1 (Weibel and Vidone 1961). The volume was measured by the water displacement method. When only one lung was available, the left lung was considered to make up 46 % of total lung volume and the right 54 %. The lungs were cut into sagittal slices and sampled so as to obtain representative samples of the lung (Langston *et al.* 1979).

Sections 5~7 μm thick obtained as above were stained with hematoxylin-eosin and observed with light microscope. Chronological changes of body weight, CR length, lung weight and volume, and lung to body weight ratio were analysed. Also observed were changes in histological characteristics of the bronchus, acinus, blood vessels, pleura and interstitial tissue by gestational age, and in 53 cases from 5 to 21 weeks, the height of epithelium at the terminal buds using a micrometer.

Gestational age was expressed as gestational weeks, the criteria being based on the time table by Moore (1978) for embryo and the CR length table by Lee (1975) for fetus. All the data were represented as mean ±one standard deviation.

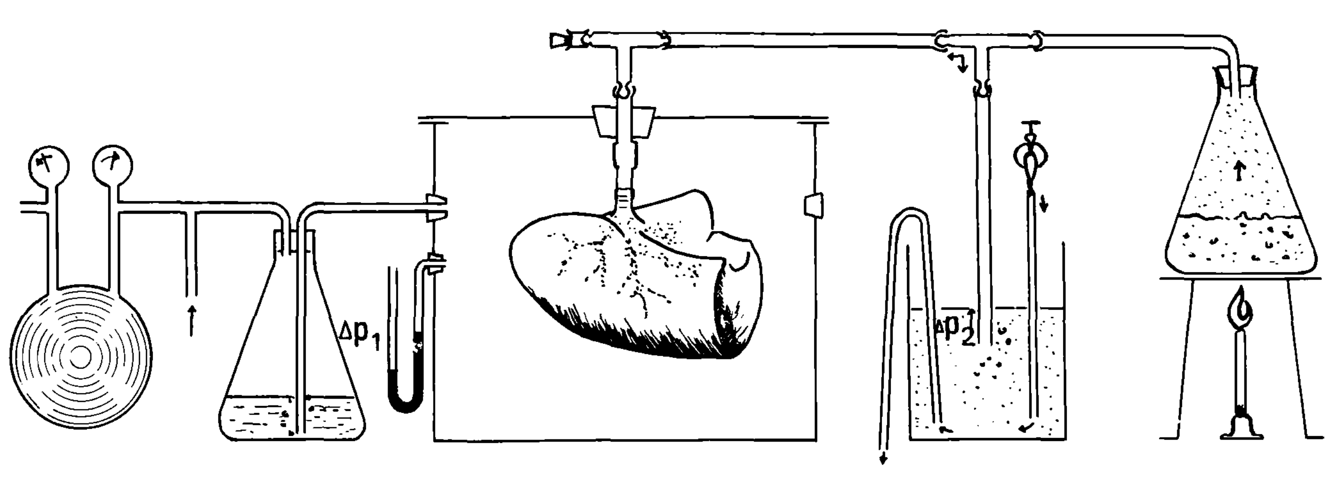

Fig. 1. Apparatus used in the fixation of lung in a controlled state of inflation (from Weibel & Vidone 1961).

RESULTS

1. The Lung Weight

The changes of body weight, crown rump (CR) length and lung weight by gestational age are illustrated in Table 1 and Fig. 2. The lung weight increased progressively from 0.7 gm at 9~12 weeks of gestational age to 45.2 gm at 37~40 weeks. The right lung made up 53~55 % (mean; 54 %) of the total lung weight. The lung to body weight ratio increased from 2.3 % at 9~12 week to 3.9 % at 13~16 weeks, and then decreased progressively to 1.9 % at 37~40 weeks (Fig. 3). The weights of various organs and their weight ratios to lung are demonstrated in Table 2 and Fig. 4. Generally, the ratios increased with advancing gestational age.

2. The Lung Volume

The volume of the lung fixed at inflated state increased rapidly at 24~25 weeks as an exponential fit, while the weight increased as a linear fit (Fig. 5).

3. Branching Patterns of the Embryonal Lung (Table 3, Fig. 6)

At 4 weeks of gestational age, tracheal bud was identified evaginating from the esophagus. Three embryos of 5 weeks showed right and left stem bronchi. At 6 weeks, lobar bronchi and, focally, segmental bronchi were visible. In 2 embryos of 7 weeks segmental bronchi were completed, one

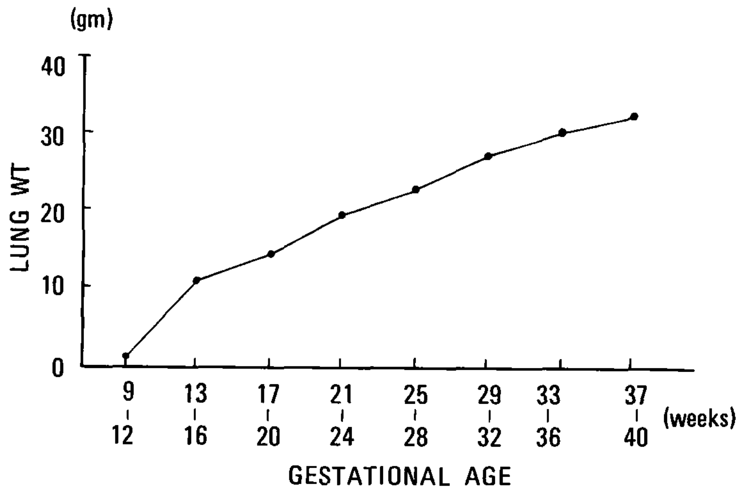

Fig. 2. Lung weight by gestational age.

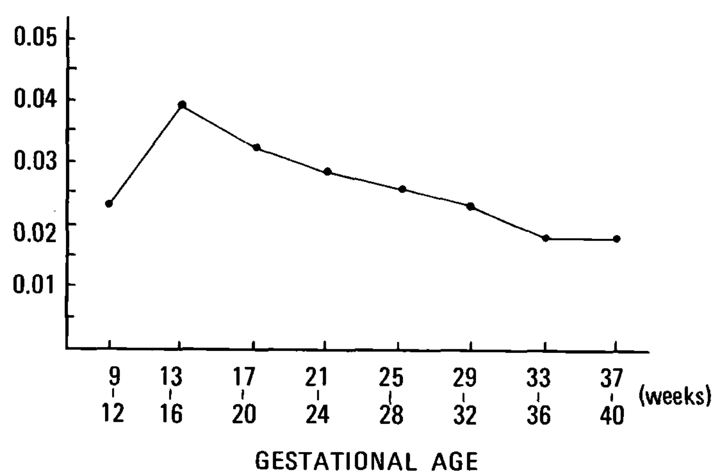

Fig. 3. Lung to body weight ratio by gestational age.

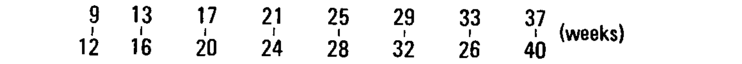

Fig. 4. Weight ratio of various organs to lung.

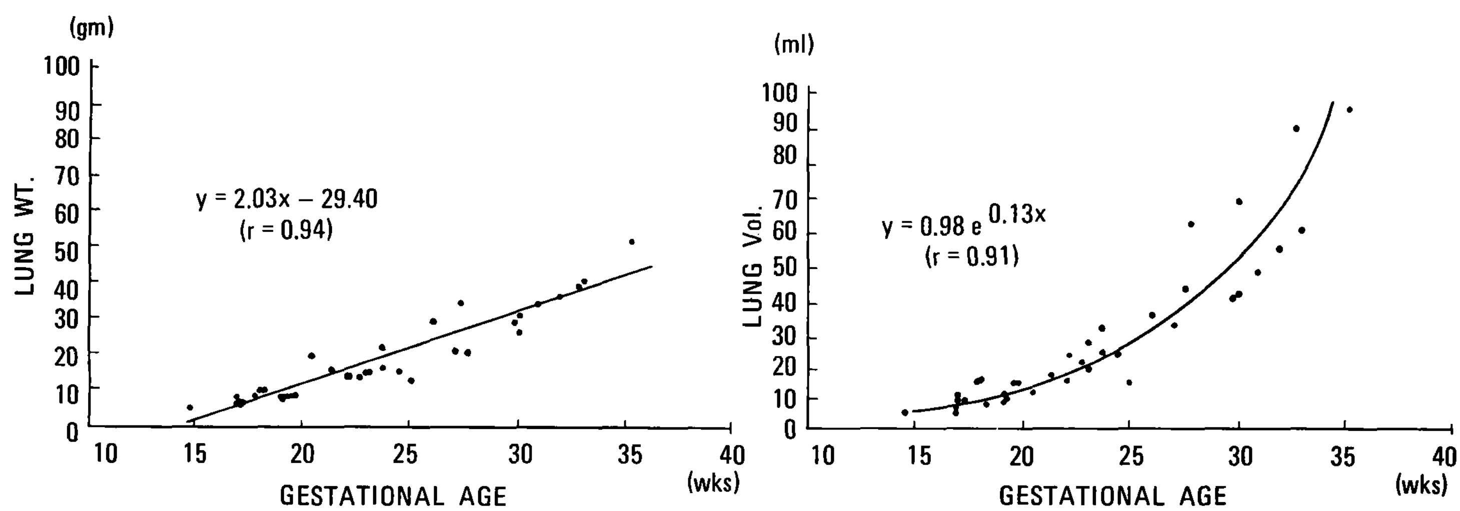

Fig. 5. Scatter diagram demonstrating increase of lung weight and volume in relation to gestational age.

Table 1. Measurements of number of fetuses by gestational age

Gestational age (weeks)	Number of cases*	Crown-Rump length (cm)	Body wt. (gm)	Lung wt. (gm)	Lung Rt/Lt ratio	Lung to body wt. ratio
4	1					
5– 8	15	1.3±0.6	0.9± 0.4			
9–12	14 (2)	5.2±1.0	13.9± 10.4	0.7±0.1	54/46	0.023
13–16	9 (8)	10.6±1.3	97.7± 49.7	3.9±1.0	54/46	0.039
17–20	36(20)	14.2±1.1	234.0± 89.1	7.5±2.4	54/46	0.032
21–24	40(38)	19.4±1.7	534.4±187.0	15.2±3.9	55/45	0.028
25–28	27(26)	22.6±1.6	912.8±199.9	24.1±5.5	55/45	0.026
29–32	22(18)	27.1±0.8	1376.0±214.9	32.0±4.4	55/45	0.023
33–36	27(27)	30.1±1.0	2015.1±327.6	37.9±4.9	55/46	0.018
37–40	7 (7)	32.6±3.2	2443.6±500.6	45.2±9.9	53/47	0.018
Total	198(146)				54/46	0.025

* Values in parenthesis represent the number of cases, in which full autopsy and organ measurements were performed.

Table 2. Weights of various organs and their weight ratios to lung

Gestational Age(weeks)	No. of cases	Lung Wt.(gm)	Kidney Wt.	Kidney ratio	Heart Wt.	Heart ratio	Spleen Wt.	Spleen ratio	Thymus Wt.	Thymus ratio	Adrenal gl. Wt.	Adrenal gl. ratio	Liver Wt.	Liver ratio
9–12	2	0.7±0.1												
13–16	8	3.9±1.0	1.3±0.5	.34	1.4±0.9	.37	0.2±0.1	.05	0.4±0.3	.12	0.8±0.5	.20	4.4± 1.9	1.14
17–20	20	7.5±2.4	2.5±0.8	.33	1.9±0.8	.26	1.3±0.1	.05	0.5±0.2	.07	1.4±0.6	.19	11.4±.3.6	1.52
21–24	38	15.2±3.9	5.3±2.0	.27	4.2±1.5	.27	0.9±0.4	.06	1.5±0.8	.10	2.8±1.3	.18	26.1±.9.0	1.72
25–28	26	24.1±5.5	9.0±2.7	.37	6.8±2.3	.28	1.8±0.7	.07	3.6±1.3	.15	3.2±0.8	.13	41.9±10.4	1.37
29–32	18	32.0±4.4	12.4±2.2	.39	10.9±1.8	.31	2.7±0.9	.08	6.9±1.8	.21	4.2±0.8	.13	57.4± 9.4	1.79
33–36	27	37.9±4.9	18.6±3.7	.49	14.5±2.9	.38	4.5±1.2	.11	10.5±3.0	.27	5.6±1.2	.15	78.1±11.9	2.06
37–40	7	45.2±9.9	21.3±5.8	.47	18.0±4.8	.39	6.4±1.5	.141	10.6±2.7	.23	6.9±2.7	.15	96.3±19.0	2.12

showing the development of subsegmental bronchi. At 8 weeks subsegmental bronchi were identified.

4. Histological Findings

4 weeks; Tracheal buds evaginating from the anterior side of the esophagus were identified, which were composed of basal lamina and 7~10 layers of cells in frequent mitoses.

5~8 weeks; Tubules were lined by pseudostratified columnar epithelium. Muscle fibers were identified around the tubules at 5 weeks, and there were cartilage centers at the stem bronchi at 8 weeks. By 5 weeks, capillary plexuses infiltrated with nucleated red blood cells appeared around the tubules and, at 8 weeks vessels became thick-walled. Interstitial cells were evenly distributed in early embryos, but by 6 weeks the cells were aggregated around the tubules.

At 6 weeks, lobes of the lungs were demarcated and cells with darkly-staining nuclei appeared at the periphery of the lung, which developed into single layer of mesothelial cells at 7 weeks.

9~12 weeks; Generally, the lung showed a glandular appearance. The tubules could be classified into three kinds according to their lining epithelium; the most proximal tubules were lined by corrugated pseudostratified columnar epithelium, the mid-portion tubules by tall columnar epithelium with hyperchromatic nucleus located near the lumen and subnuclear vacuoles. The terminal buds, the most distal part, were lined by columnar epithelium with less basophilic nucleus located at the midportion of the cells and sub- and supranuclear vacuoles. These patterns appeared at 9 weeks and were distinct by 10 weeks. By 11 weeks, loose connective tissue was developing beneath the mesothelial cell layer, and was invading the parenchyme and leading to lobulation. The tubules with hyperchromatic nuclei were located at the center of

Table 3. Branching levels in 12 embryos

Gestational Age (wks)	Crown-Rump length (mm)	Streeter's develop-mental horizon	Branching level
4		XII	lung bud
5	5.6	XIV	stem bronchus*
	6.0	XV	stem bronchus
	7.8	XV	stem bronchus
6	9.0	XVI	segmental bronchus (incomplete)
	11.0	XVII	segmental bronchus* (incomplete)
	11.4	XVII	segmental bronchus (incomplete)
7	14.0	XVIII	segmental bronchus (complete)
	15.0	XVIII	segmental bronchus partly subsegmental*
8	19.8	XX	subsegmental bronchus
	20.0	XXI	subsegmental bronchus*
	23.6	XXII	subsegmental bronchus

* Schematic reconstruction diagrams are given in Fig. 6.

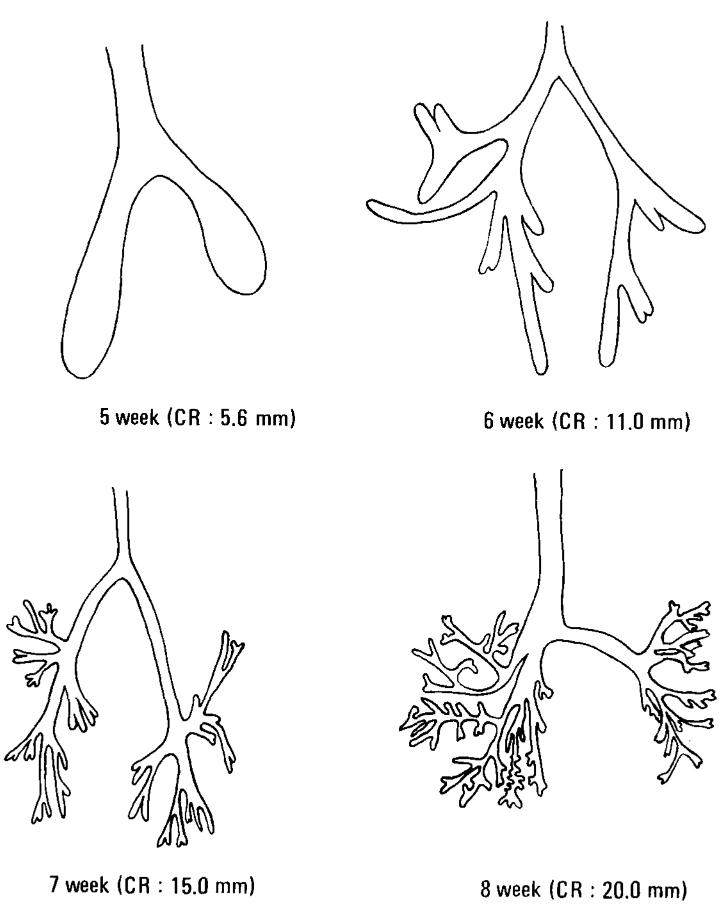

Fig. 6. Schematic reconstruction of branching patterns of embryos.

the lobules, while tubules with less basophilic nuclei were at the periphery. Cartilage and a layer of smooth muscle were developing in the large bronchi, and muscle fibers were identified around the tubules with hyperchromatic nuclei.

Arteries and veins were noted around the large bronchi and loose connective tissue, and the capillary plexuses were visible among the condensed interstitial cells, especially around the terminal buds. The interstitial cells were edematous in appearance and still aggregated around the tubules. Frequent mitoses of the interstitiai and tubule-lining cells were observed.

13～16 weeks; The proliferating tubules crowded the interstitial tissue, the tubules with hyperchromatic nuclei decreasing in proportion. A muscle layer, semicircular cartilage, and primitive mucous glands with acini were seen in the large bronchial walls. The bronchial epithelium was ciliated and corrugated with a connective tissue core. By 16 weeks, the interstitial cells decreased in their aggregation around the tubules, and frequent mitoses of the tubular and interstitial cells were seen. The loose connective tissue beneath the mesothelial layer increased in thickness.

17～20 weeks; There was further development of mucous glands in the bronchial wall, and cilia were noted at the lining epithelium of the bronchioles, thereby defining the terminal bronchioles. By 18 weeks, as the lining cells of the distal tubules began to flatten, the lungs gradually began to lose their glandular appearance. The canalicular structure with irregular lumen progressively increased in number and the lining epithelium showed a decreasing number of vacuoles.

Dilated capillaries were occasionally seen in the interstitium, becoming more prominent around the tubules with focal invasion of the capillaries between the epithelia and air-blood-barrier formation by 17 weeks. The condensation phenomenon of the interstitial cells was no longer evident.

21～24 weeks; Well-developed cartilage appeared in the peripheral bronchial wall. Canals with irregular lumen and cells with attenuated cytoplasm increased markedly, the cytoplasmal attenuation starting from the proximal part of the acinus. As a result, tubules with round lumen and cuboidal epithelium decreased progressively.

Numerous air-blood-barriers were formed as capillaries further proliferated and invaded between the epithelia. Foci of extramedullary hemopoiesis was also noted.

25~28 weeks; As the attenuation of the cytoplasm and luminal irregularities increased, the canals were wavy or tortous in appearance, and papilliform projections into air spaces were noted. Capillaries were further proliferating, occasionally protruding markedly into the air spaces. The interstitium began to thin out and extramedullary hemopoiesis was no longer evident.

29~32 weeks; The papilliform projections increased in number and secondary crests began to appear. Occasionally proteinaceous materials were observed in the air spaces. There was further proliferation of capillaries. Much of the interstitium as well as the pleura by the expanding lung were markedly thinned out.

33~36 weeks; As the number and height of the secondary crests increased, the primitive alveoli were identified between the secondary crests as shallow depressed area. Proteinaceous materials and alveolar macrophages were identified in the air space. Occasionally foamy and plump cells thought to be type II pneumocytes were seen in the lining epithelia. There was further thinning of interstitial tissues and capillary proliferation, the capillaries appearing in a double structure.

37~40 weeks; Alveoli with delicate septum and single capillary structure were identified in all cases, but their proportion to saccules was variable in each specimen. The subpleural area was somewhat delayed in maturation and the air spaces still contained amniotic fluid and proteninaceous materials.

5. The Height of Epithelium at the Terminal Buds

The height of epithelium at the terminal buds decreased from 33.7~37.9 μm at 5 weeks to 9.5 ~10.8 μm at 21 weeks (Fig. 7).

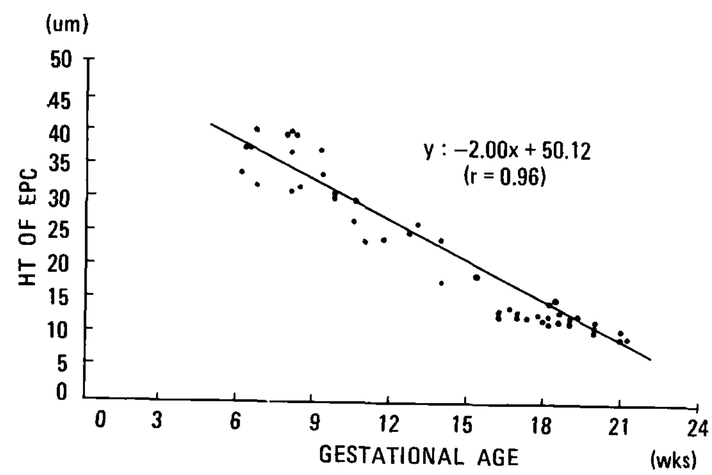

Fig. 7. Correlation between age and height of epithelium around the terminal buds.

DISCUSSION

According to the generally accepted scheme of lung growth in utero there is an early period of budding and branching in the embryonic period during which the lung buds and main and lobar bronchi are formed. During the pseudoglandular period branching of conducting airways is completed and terminal bronchioles can be identified, soon followed by the canalicular period when pulmonary acini are laid down with vascularization and flattening of the lining epithelium resulting in the formation of saccules. During the saccular period, the saccules are differentiated into alveoli by a process of more thinning of the interstitial septum, further proliferation of capillaries, and formation of the secondary crests, thereby defining the alveolar period.

Initiallly, it is difficult to distinguish the alveoli from the saccules. The alveoli can be defined morphologically as thin-walled, flask-shaped or multifaceted polygonal structures with single capillary network, while saccules contain a round space of larger size with double capillary structure. The secondary crests consist of a covering of type I alveolar epithelium and a core of interstitial cells, capillaries and connective tissue.

We attempted to describe the histological characteristics of the fetal lung with special emphasis on the sequential development of the functional respiratory unit. The degree of development was best assessed with longitudinal sections of bronchi or acini, especially around the terminal buds.

From 5 to 8 weeks all of the tubules were lined by pseudostratified columnar epithelium, and between 9 to 16 weeks, the most proximal part by pseudostratified columnar epithelium, and the mid-portion tubules proximal to the terminal buds by tall columnar epithelium. These lining epithelia and the muscle fibers around the tubules suggested that these tubules will give rise to the conducting airways. By 16 weeks, branching of the bronchioles is completed. After birth, along some of the pathways the terminal bronchioles may be transformed into an extra generation of respiratory bronchiole by 'centripetal alveolarization' and thereby the number of terminal bronchiole may decrease (Boyden and Tompsett 1965).

In some cases by 17 weeks and all by 18 weeks, cilia were identified in the tubules lined by tall columnar epithelium with hyperchromatic nucleus which served as evidence that these tubules were the future conducting airways. From 17 weeks, canalicular structure distal to the conducting airways with cilia increased progressively, which supported the fact that acini proliferated from 16~17 weeks (Hislop and Reid 1975). As acini proliferated the lumina of the canalicular structure were rather irregular compared to the straight lumina of conducting airways on longitudinal section.

By the end of 17~20 weeks, flattening of the epithelium and vascularizaiton followed the proliferation of acini. Thurlbeck (1975) also reported that epithelial flattening began at 16 weeks, vascularizaiton at 19 weeks, while these changes were observed after 20 weeks by Gandy *et al.* (1970).

With further proliferation of acini, flattening of epithelium, and vascularization during the period of 21~24 weeks and 25~28 weeks, saccules were identified. During the period of 29~32 weeks secondary crests were observed arising from the saccular wall. During 33~36 weeks, secondary crests developed further with increase in height and number accompanied by further thinning of interstitium. In all of the lungs of 37~40 weeks, alveoli with delicate septum and single capillary structure were more or less identified.

According to the reconstruction study (Hislop and Reid 1975), an acinus at birth consists of three generations of respiratory bronchiole, one of transitional duct, three of saccules and a terminal saccule, though in different acini more or fewer may be identified. As alveoli differentiate from the saccules, the saccules then convert into alveolar ducts.

It has been suggested by some investigators that alveoli are absent at birth (Reid 1967; Boyden 1969); others have found alveoli at birth, the number varying as 17×10^6 (Davies and Reid 1970), 20×10^6 (Dunnil 1962), or 71×10^6 (Thurlbeck 1975). These conflicting data probably arise from three main reasons (Thurlbeck 1975); biologic variation, differences in preparation of tissue for examination, and difficulty in defining and recognizing alveoli. In the present study we could identify alveoli in all cases over 37 weeks of gestation, but there was marked individual variation in their proportion to saccules.

It is interesting that the height of epithelium at the terminal buds decreased progressively from 5 weeks to 21 weeks, which suggested that the epithelium of brochus, bronchiole or acinus were different from each other since the early stage of differentiation.

The volume to which the lung is inflated may alter the dimensions of structure within it, and it is therefore important to indicate this volume when making quantitative measurements of lung structure. Various techniques have been used to inflate lungs at autopsy, for example, expansion to apparent full inflation (Moolten 1935; Leopold and Gough 1957), to an estimated 0.75 of full inflation (Weibel and Vidone 1961), to the size of a thorax at necropsy (Hartcroft and Macklin 1943; McLean 1956), or to standard transpulmonary pressure (Heard 1960). Thurlbeck (1979) concluded that the volume of lungs fixed with formaldehyde at a transpulmonary pressure of 25 cm H_2O closely approximates total lung capacity. We therefore used 24~25 cm H_2O of negative pressure in the inflation of the fetal lung.

Two methods are commonly used for inflating the lung for study of morphometry or structure. One is to give intrabronchial positive pressure with formalin solution for more than 12 hours (Heard 1960), and the other is to inflate with negative pressure and provide formalin vapor for 1~2 hour (Weibel and Vidone 1961). In the former, fluid will reduce surface forces and perhaps result in overdistension at conventional distending transpulmonary pressure of 20~30 cm H_2O, while fixation may harden lung tissue and cause tissue shrinkage and thus produce smaller lung volumes. The latter, on the other hand, is more physiologic. The lung volume increased rapidly from 24~25 weeks, which coincided with proliferation of the acini and thinning of the interstitial septum.

Reconstruction studies of the embryonal lungs revealed the critical period in gestation when segments were being formed, and had provided the rational explanation for certain variations of bronchial trees and pulmonary vessels (Well and Boyden 1954). In Streeter's developmental horizon XVII, the development of segmental bronchi is usually completed (Streeter 1948; Well and Boyden 1954), but two cases in the present study showed a delay in development.

The mode of bronchial division is still disputed, some regarding all growth as proceeding from the growing tip, others considering that lateral branching takes place proximal to the tip. According to Arey (1946), both methods occur.

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LEGENDS FOR PLATES

Plate 1. 4 weeks (GA). Lung bud anterior to the esopnagus is seen, which is lined by 7∼10 layers of epithelial cells. H & E ×100

Plate 2. 5 weeks (GA). Stem bronchi are identified in both lungs, which are lined by pseudostratified columnar epithelium. Interstitial cells are even in distribution. H & E ×40

Plate 3. 6 weeks (GA). Tubules are lined by pseudostratified columnar epithelium, and interstitial cells begin to condence around the tubules. H & E ×360

Plate 4. 8 weeks (GA). Cartilage centers are seen in the proximal portion of stem bonchi. Lobar septum is visible, which is evident from the 6th week of gestation. H & E ×40

Plate 5. 9 weeks (GA). Mid-portion tubules are lined by tall columnar epithelium, whose nuclei are hyperchromatic, and located near the lumen with subnuclear clearing, while more distal tubules are lined by columnar cells, with less basophilic nuclei, located at mid-portion of the cells. H & E ×40

Plate 6. 9 weeks (GA). Higher power view of mid-portion tubules of plate 5. Interstitial cells are aggregated around the tubules. H & E ×360

Plate 7. 11 weeks (GA). Loose connective tissue develops below the mesothelial cell layer of the pleura, which invades the parenchyme and leads to lobulation. H & E ×40

Plate 8. 12 weeks (GA). Two kinds of tubules are seen as in plate 5. Terminal buds appear as clumping of nuclei. Aggregations of interstitial cells around the tubules are remarkable. H & E ×100

Plate 9. 14 weeks (GA). Lobulation is accentuated, and tubules are crowded. Bronchial epithelia are corrugated with connective tissue core, and cartilage is seen in the wall of peripheral bronchus. H & E ×40

Plate 10. 16 weeks (GA). Condensation of interstitial cells around the tubules begins to disappear. Distal tubules are lined by cuboidal epithelia. H & E ×100

Plate 11-12. 19 weeks (GA). Lumina of canals are somewhat irregular, and the lining epithelia are partly attenuated. These canals lose glandular appearance. Cilia are seen at the epithelia of terminal bronchioles. H & E × 40, ×100

Plate 13. 22 weeks (GA). Most canals are irregular in outline, and rqund canals with uniform cuboidal cells are rare. Conducting airways stain deeply. H & E ×40

Plate 14. 24 weeks (GA). Most lining cells are attenuated and air-blood-barriers are numerous. H & E ×100

Plate 15. 26 weeks (GA). Canalicular walls are wavy or tortuous and the septa begin to thin out. H & E ×40

Plate 16. 27 weeks (GA). There are numerous air-blood-barriers, and capillaries are sometimes protruded markedly into air space. H & E ×360

Plate 17. 30 weeks (GA). Papilliform projections are seen . There are numerous air-blood-barriers with protrusion into air space. H & E ×360

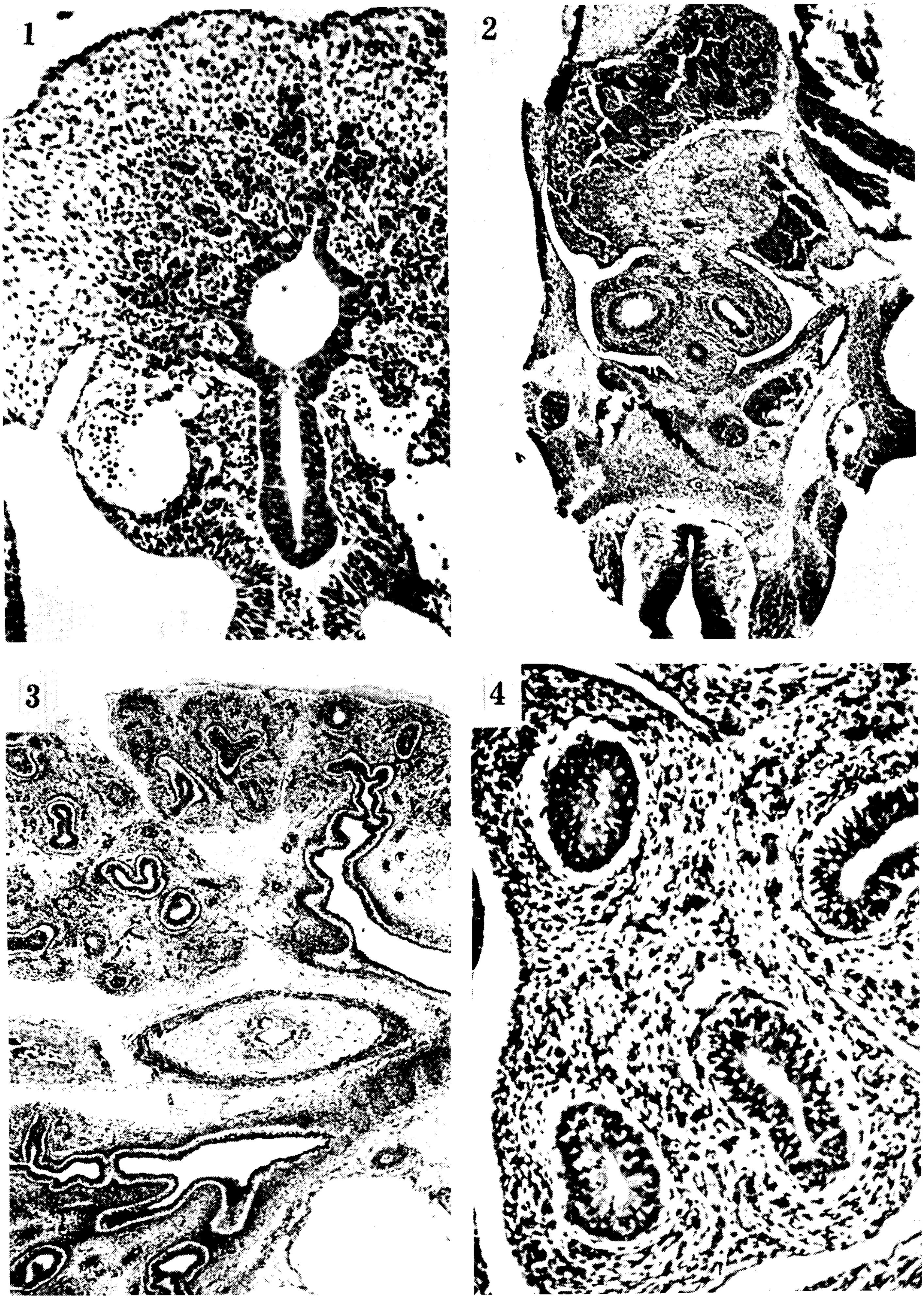
Plate 18. 32 weeks (GA). Branching pattern of acini is seen. There are a few secondary crests. Septa are thinned out considerably. H & E ×40

Plate 19. 35 weeks (GA). Secondary crests are weell developed, showing increase in number and height. H & E ×40

Plate 20. 35 weeks (GA). Higher power view of secondary crests and septa. Secondary crests contain capillaries and interstitial cells. The depressed area between secondary crests are primitive alveoli. H & E ×360

Plate 21. 37 weeks (GA). Secondary crests are further developed, and alveoli are identified. H & E ×40

Plate 22. 38 weeks (GA). Septa are delicate and a few well developed alveoli are defined. H & E ×100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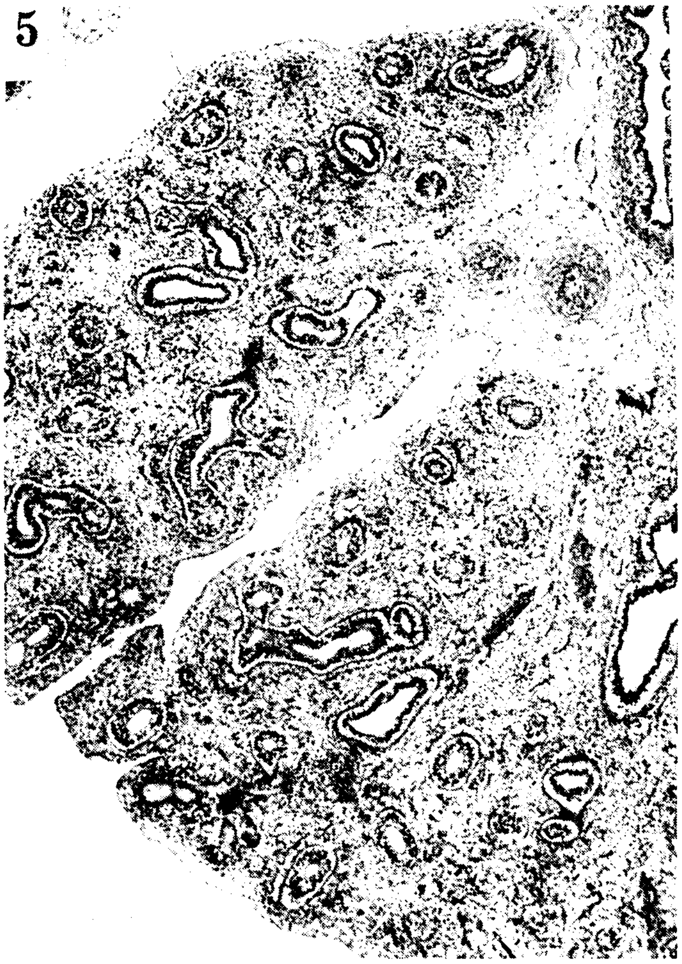
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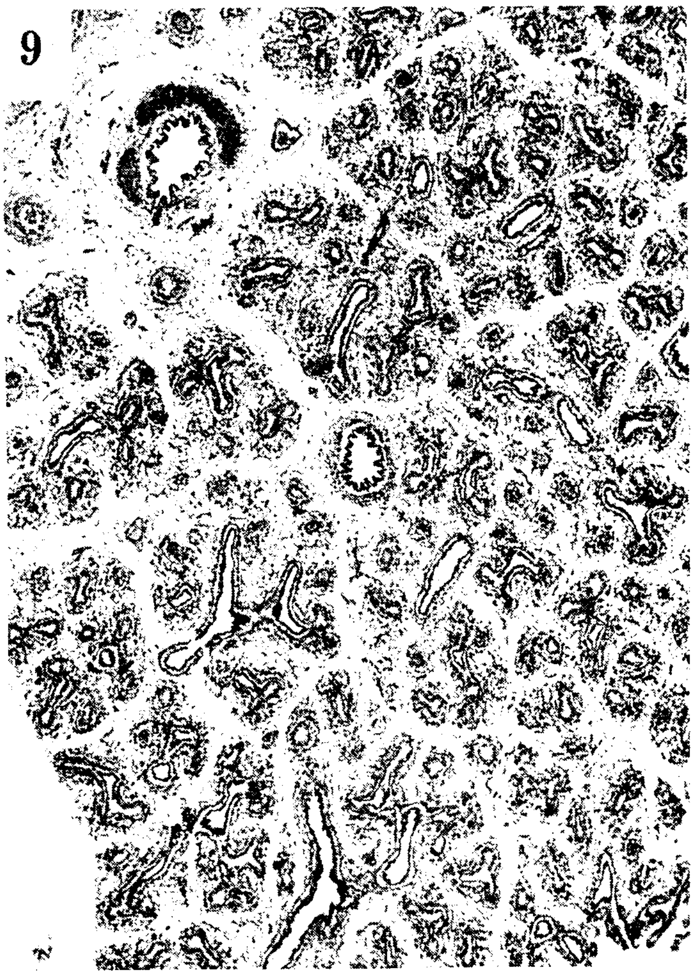

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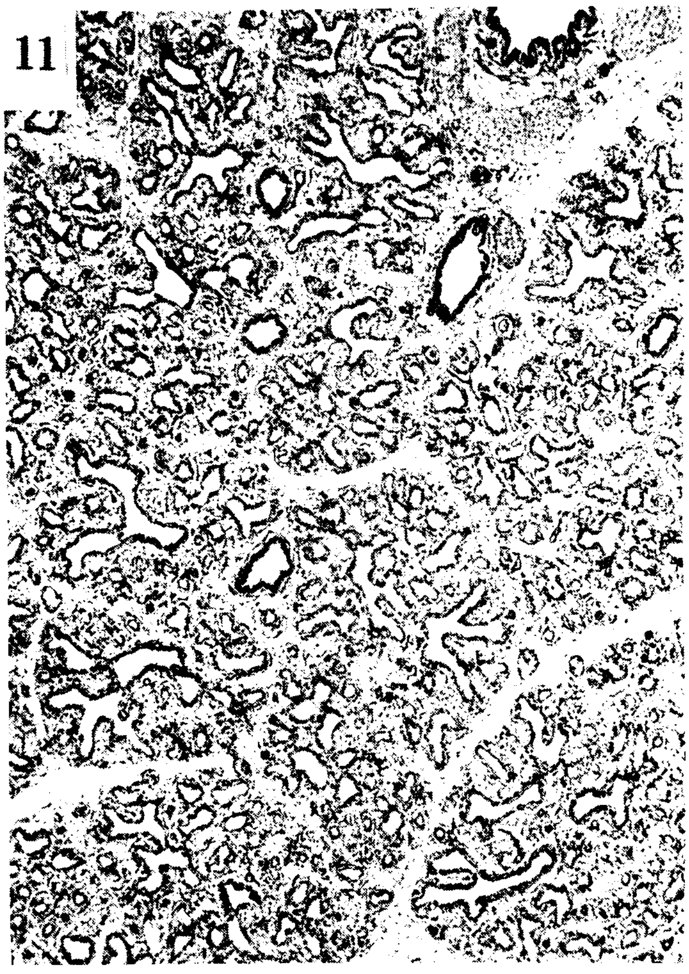

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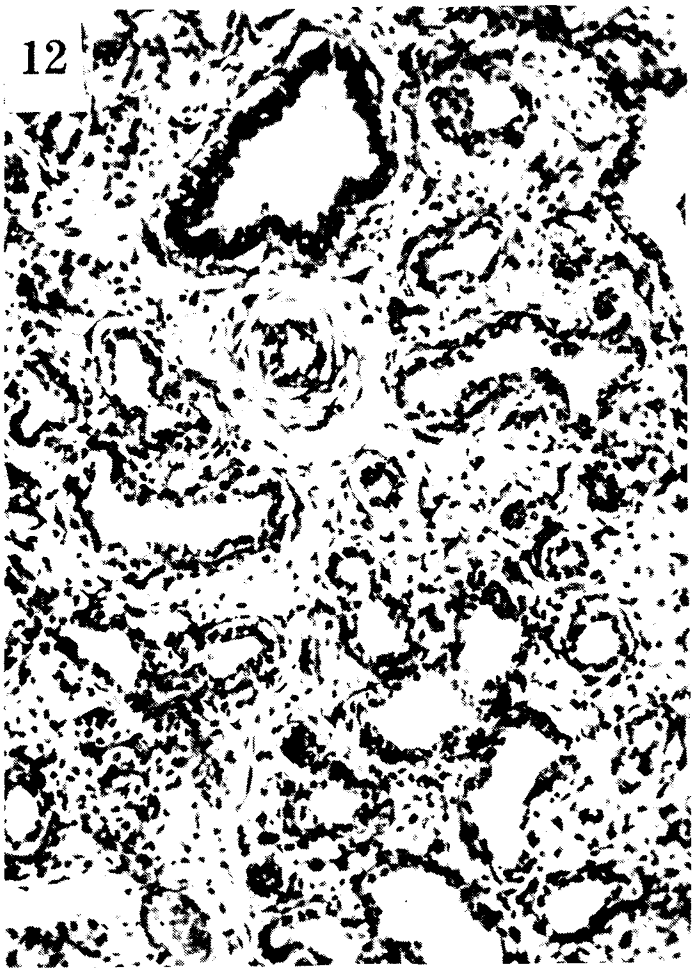


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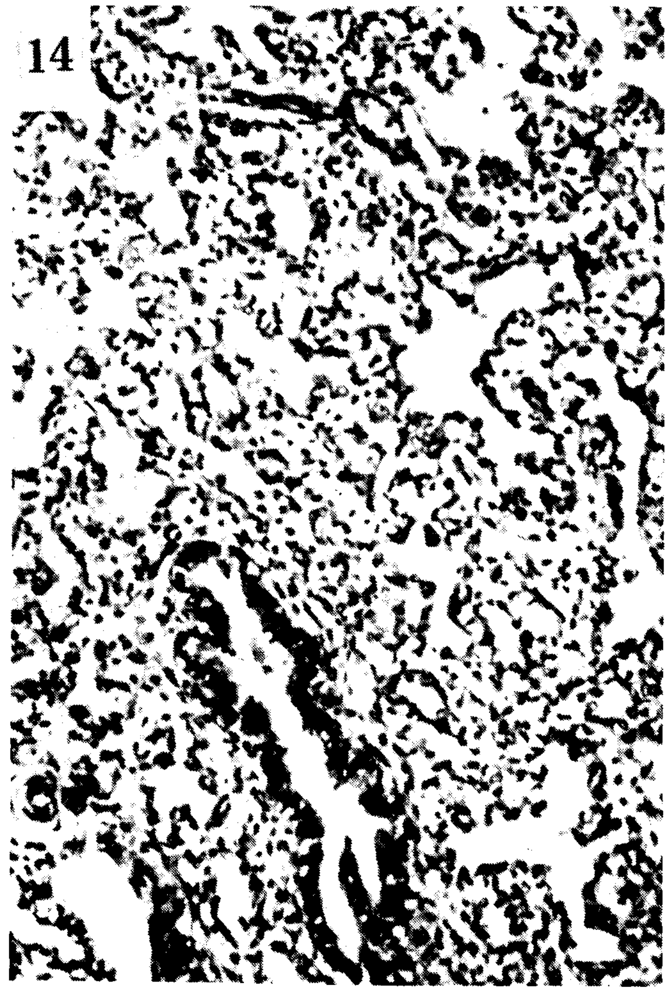
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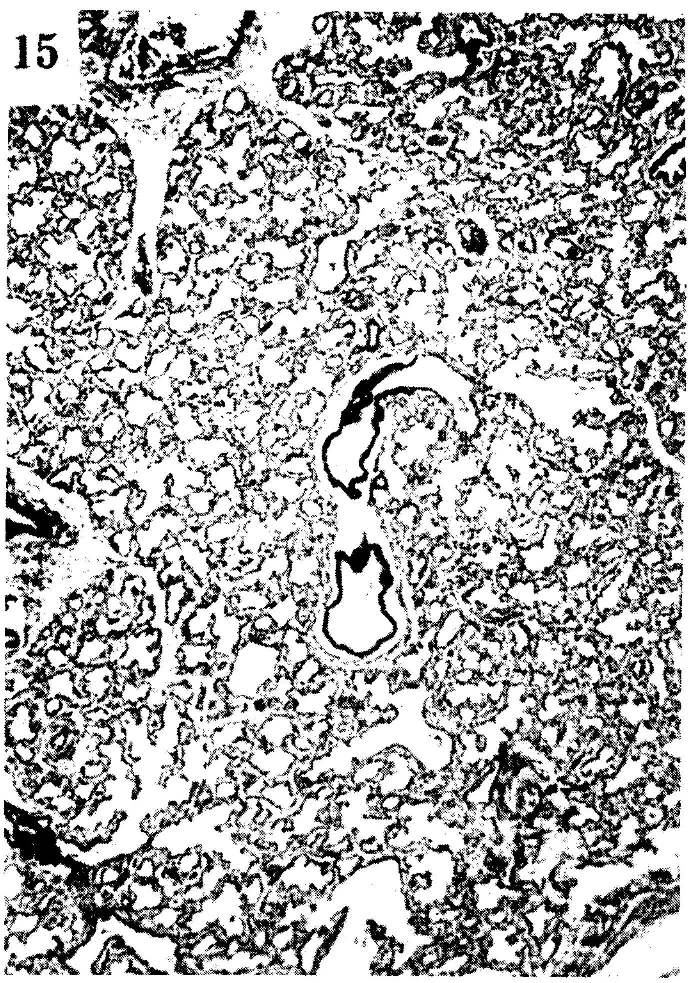
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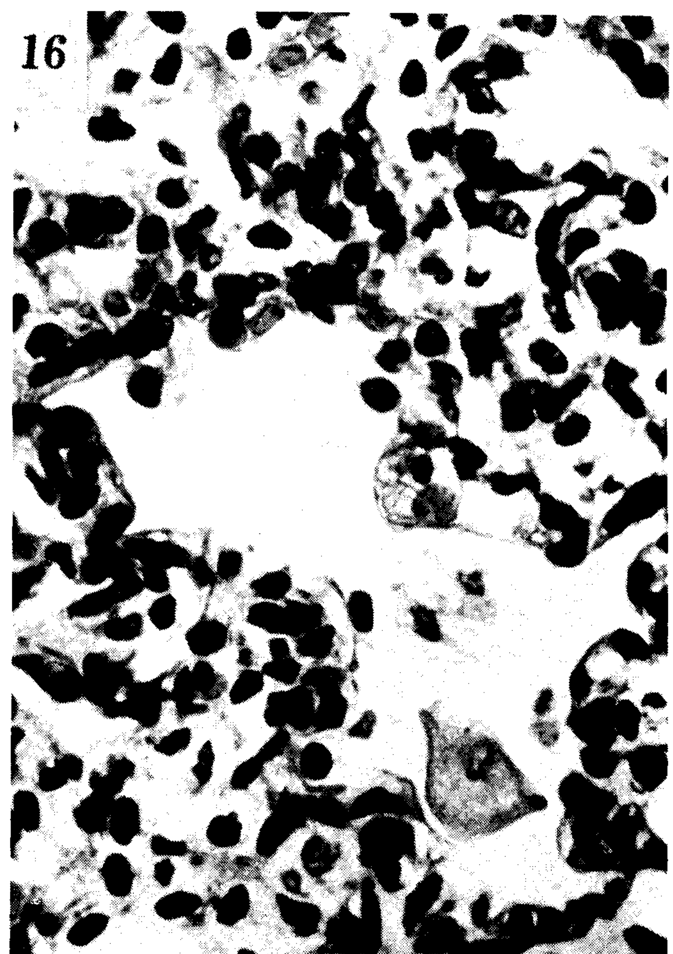
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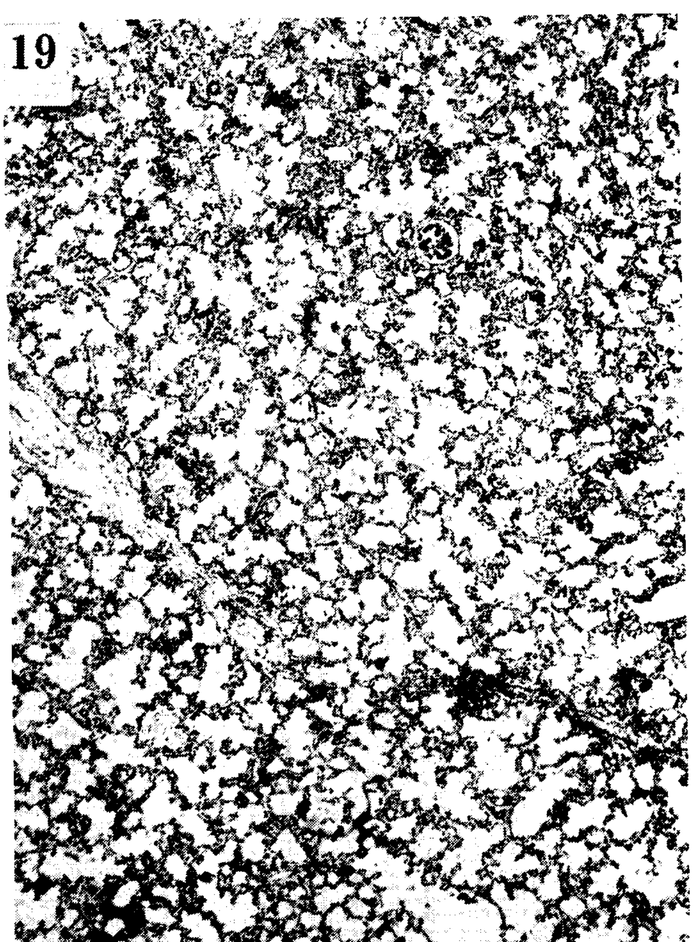
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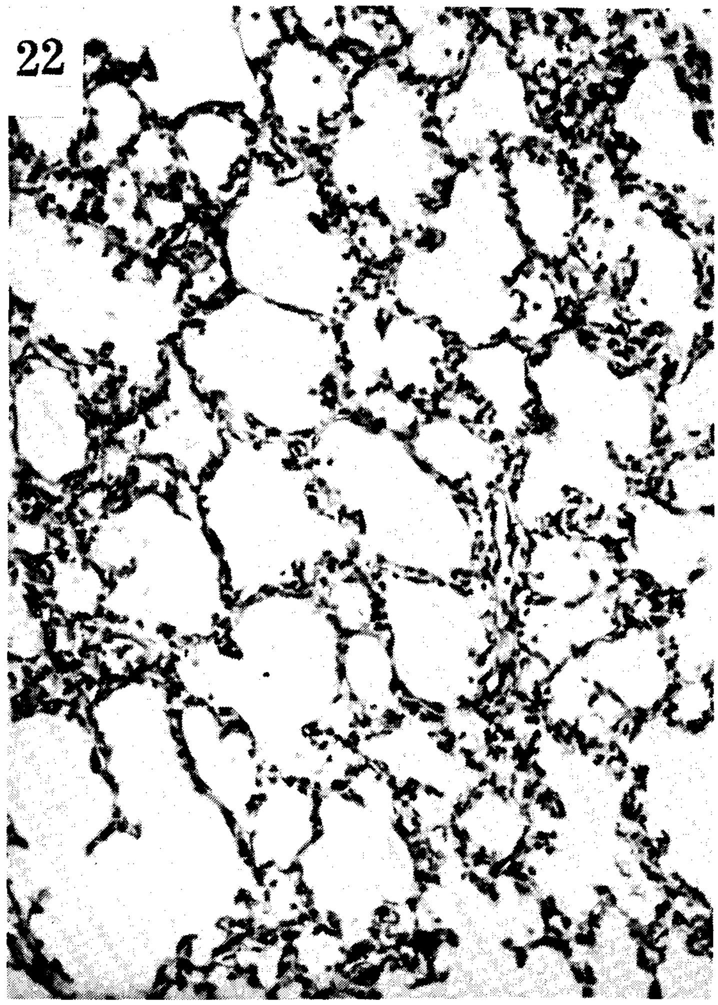
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= 국문초록 =

韓國人 胎兒肺의 形態學的 發育에 關한 硏究

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韓國人 배아 16例 및 胎兒 182例等 總 198例에 對하여 肺의 重量, 容積, 배아기관지의 分枝樣狀 및 組織學的 所見等을 觀察하였다.

1. 肺의 重量은 9~12 週齡에 0.7 gm에서 37~40 週齡에 45.2 gm으로 점진적으로 증가하였으며, 右側肺가 차지하는 比率은 平均 54%이었다. 體重에 대한 肺重量의 比率은 9~12 週齡에 2.3%에서 13~16 週齡에 3.9%로 증가하였다가, 이후에는 37~40 週齡에 1.8%로 점점 감소하였다.

2. 24~25 cm H_2O의 陰壓으로 膨脹시킨 狀態에서 固定시킨 肺의 容積은 24~25 週齡부터 급격히 증가하였다.

3. 배아의 氣管支는 4 週齡에 肺芽, 5 週齡에 幹氣管支, 6週齡에 分節支, 7週齡에 亞分節支까지 발달하였다.

4. 組織學的 所見은 一括하여 16週齡까지는 주로 空氣傳導管, 以後에는 주로 呼吸性組織이 發達하였다.

1) 4~8週齡 : 小管이 僞重層圓柱上皮로 裏裝되어 氣管支가 分枝하는 것을 알 수 있었다. 6 週齡부터 大葉이 形成되고 間質細胞는 小管周圍에 濃縮되는 傾向을 보였으며, 7週齡에는 中皮細胞 單一層의 肋膜이 형성되었으며, 8週齡에는 幹氣管支의 起始部에 軟骨中心이 認知되었다.

2) 9~16週齡 : 주로細氣管支가 발달하며, 肺는 전체적으로 腺形을 나타내었다. 11週부터 肋膜의 中皮細胞層밑에 느슨한 結締組織이 나타나며 이에 의해 肺의 小葉化가 일어났다. 主氣管支의 上皮에 纖毛가 나타나며, 壁에 細葉을 가진 粘液腺이 나타나며, 末期에는 間質細胞의 濃縮現象이 없어졌다.

3)17~28週齡 : 細葉의 증식 및 이어서 細葉上皮의 扁平化, 細葉의 血管化가 일어나 末期에는 小囊이 형성되었다. 氣管支壁의 軟骨 및 粘液腺이 成熟되며, 細氣管支까지 纖毛가 나타나 終末氣管支를 인지할 수 있었다.

4) 29~36週齡 : 小囊이 더욱 증가하고 中隔이 점점 얇아졌다. 2次稜이나타나 小囊을 細分化하였다. 氣空內에 蛋白性 物質 및 大食細胞가 나타났다.

5) 37~40週齡 : 부분적으로微細한 中隔과 單一毛細血管構造를 가진 肺胞가 나타난다.

5. 終蕾部位의 上皮의 높이가 5週齡에 36 μm에서 21週齡에 9.8 μm로 감소하였다.