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The Influence of Pulmonary Growth and Development on Paediatric Respiratory Diseases

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The mortality, morbidity and symptomatology of respiratory diseases in infants and children may be partially related to age specific phenomena of structure and function. Such are the comparatively smaller functional residual capacity and respiratory surface area; the difference in growth velocity of alveolar numbers and size; the smaller number of intrapulmonary communications; the larger resistance of the peripheral airways accentuated by fewer muscular elements and larger number of mucous glands in the same; and the smaller elastic recoil pressure of the lung in children as compared to adults. Many factors compensate, partially or totally, for these apparent handicaps, but the influence of growth and development on disease processes can certainly not be disregarded.

The importance of respiratory diseases in infants and children hardly needs to be emphasized. Although morbidity statistics in this respect are not very precise, the number of acute respiratory diseases in children below the age of 17 was estimated to make up 60% of all illnesses (school days missed for the same reason was 51% of all), and chronic respiratory conditions including asthma and cystic fibrosis, are responsible for about half of all chronic ailments in that age. The mortality figures are more reliable and no less significant. Approximately 30% of all deaths in the newborn period, 10% in children 1 to 4 years of age, and 25% of those between 5 and 14 years, are due to respiratory diseases.

Besides the frequency of these conditions, the symptoms of various respiratory diseases tend to be more severe in infants and children and, in fact, they more frequently lead to emergency situations. Another well-known fact is that some diseases, e.g. respiratory distress syndrome and bronchiolitis, are specifically related to certain paediatric age groups.

The assumption that age-related structural and physiological characteristics of the respiratory system could be the cause of some of these phenomena is inescapable. This article is an attempt to provide some answers to the question.

Before searching for those anatomic-physiologic properties of young age, one must enumerate respiratory functions, the impairment of which generally causes the most significant symptoms. These are:

A. Abnormal elastic properties of the lung and/or the thorax;

B. abnormal patency of the airways, such as obstruction of the upper and/or of the lower airways;

C. abnormal relationships of ventilation and perfusion in various parts of the lung; and, finally,

D. impaired gas diffusion through increased barriers and/or owing to a decreased capillary surface area for gas exchange.

A and B type abnormalities result in laboured respiration and hypoventilation, which eventually leads to respiratory insufficiency, whereas C and D more directly interfere with the normal exchange of oxygen and carbon dioxide, thus being another cause of insufficiency or failure. A combination of all four causes, a not too infrequent possibility, may result in desperate respiratory emergencies.

According to our assumption, let us examine the age-specific properties of the respiratory system along these lines.

It must be understood that "age specificity" is another name for phenomena related to *growth and development*. Structure and function of the whole body, as well as of individual organ systems, grow according to rules which are usually expressed in mathematical terms and presented in growth charts. By definition, these presentations are simplified, and small, but sometimes very significant, irregularities of the growth patterns are being "smoothed out". It is often precisely one or another such irregularity that is responsible for the unexpected behaviour of a system in a specific age.

The overall *growth of the lung* is usually defined by changes of lung volume with age, or more precisely with body height. The volume best reflecting this growth is functional residual capacity, i.e., the volume the lung assumes at its resting position at the end of a normal expiration. This volume is determined largely by the balance between the opposing elastic recoil forces of the lung and thorax. Fig. 1 shows the different relationship of these forces in newborns and adults, and the resulting difference between resting volume (FRC) to total volume. The comparatively smaller FRC in infants (the relationship changes gradually with advancing age), means that a young child has a relatively smaller amount of "buffer-gas" in his lung, which is a disadvantage in balancing sudden changes of respiratory gas concentrations, and it also increases the tendency of the lung to develop atelectasis, a well-known phenomenon in RDS, asthma and many other lung diseases.

Lung growth itself, of course, depends largely on the *growth of the total alveolar space*. Alveoli first appear in the human foetus at the 24th week of gestation, and they multiply rapidly during late gestation and in early childhood. At birth, the infant's lungs contain about 20 million alveoli. There are about 200 million at the end of the first year, and the final number of about 300 million is reached around 8 years of age. Beyond that it is only

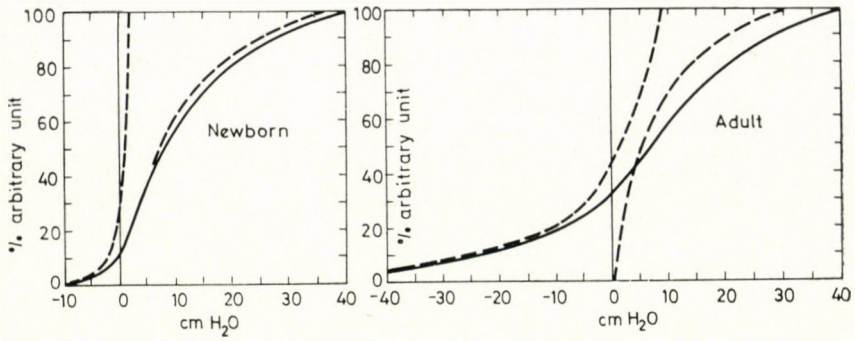

FIG. 1. Schematic diagrams to illustrate the main changes of the volume pressure curves of the respiratory system occurring during growth. The resting volume of the lung, i.e., functional residual capacity, is at the level where the solid line crosses the vertical line through zero pressure, at which point the opposing elastic pressures of the thorax (broken line to the left), and the one of the lung (broken line to the right) are equal on either side of zero pressure. It is evident that in a newborn this volume constitutes a smaller percentage of the total volume than in adults. (E. Agostoni and J. Mead, Statics of the Respiratory System, In: Handbook of Physiology, Chapter 13, Respiration, Vol. 1, W. O. Fenn and H. Rahn (eds). American Physiological Society, Washington, D. C. 1964)

the increasing size of the alveoli that contributes to further lung growth. The growth curve for alveolar size is different from that for the numbers. At first the alveoli are relatively large and shallow. Within a few months after birth they take a rounded form, their radii become smaller, but this ensures a larger total surface area. From here on the growth of alveolar diameter is reasonably linear and continuous until body growth is completed.

The fact that *respiratory surface area*, as related to body weight, almost doubles by 1½ years and triples by 3 years of age, means that a young child has a smaller reserve surface for gas exchange than an older one. He evidently does not need the same reserves; he will not have to do heavy exercise. On the other hand, he may have to work quite hard to keep breathing when suffering from a respiratory ailment which impairs the mechanics of breathing. If, owing to some lung disease, his gas exchange surface is already smaller than normal, this may lead to a catastrophe. There are cases where the energy required for the work of breathing alone is more than can be provided altogether; thus the small alveolar surface area of the lung in young children may become a dangerous handicap.

The characteristic growth curve for the number of alveoli has a distinct influence on the reconstructive properties of the lung after injury, on the one hand, and on faulty development because of outside physical limitations, on the other. An example of the former would be a case of staphylococcal pneumonia causing large destruction at an early age; it can be repaired to a great extent because the number of alveoli increase greatly until 8 years of age. If, however, a thoracic deformity such as congenital

kyphoscoliosis, encroaches upon the space in which the lung can grow, the individual may end up as an adult with a total number of alveoli on the affected side, which would normally be found in a 2-year-old child.

While discussing alveolar growth patterns it seems appropriate to mention an old anatomical observation which has lately received much renewed attention. This concerns the *communications between adjacent alveoli*, alveolar ducts, alveolar bronchioles, and even between segments of the lung. Some of these channels are identical with the old pores of Kohn, others have recently been described in detail, based on scanning electron microscopic pictures. It has been discovered that these communications actually serve an important function in diseased states where, by collateral ventilation, blocks in the normal air conducting system to the alveoli can be bypassed. From the point of view of the young child, the interesting observation is that he possesses fewer communications and therefore has lesser capacity for collateral ventilation. Could this be another reason for the infant being prone to develop atelectasis? In looking for other properties of children's respiratory system, we have to examine the *growth pattern of the airways*, the obstruction of which can cause so much difficulty. In contrast to the alveoli, the number of bronchi does not increase beyond the 16th week of gestational age. Thus the bronchial tree is a miniature of the adult one, at least as the number of branchings is concerned; not, however, in respect to the relative size of the airways. While all bronchi are naturally much smaller in infants and children than in adults, they are not sealed down proportionately to body size. If they were, their very high resistance would make breathing impossible. As it is, their total resistance is such that the energy required to breathe the normal amount of air per minute is the same in a newborn baby as in an adult.

The size (diameter) of various parts of the air-conducting system grows on different scales. Fig. 2 shows that while the tracheal diameter increases threefold between birth and adult age, that of the bronchioles only doubles. While this would make us think that the resistance of the peripheral, small airways in a young child might be relatively less than later, it seems that the opposite is true. For some reason, probably related to the length and cross-section area of this complicated tubing system, the peripheral bronchi have in fact a relatively larger resistance in children below the age of 5. After this age, a sudden increase of the same occurs. One can thus hardly escape the conclusion that a child younger than 5 must have more trouble with peripheral airway diseases than an older one. Indeed, bronchiolitis in its severe clinical form is a disease of the infant and young child, and if present in older ones, it may not be noticeable clinically.

There are further facts related to the *partition of airway resistance* which point to differences between individuals of various ages. It is known

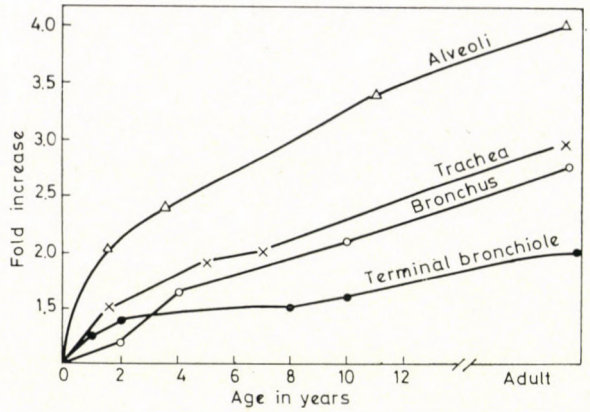

FIG. 2. Schema of changes in airway diameters with age (Handbook of Respiration, W. B. Saunders Co., Philadelphia 1958, Data of Scammon and Engel)

that in an adult the resistance of the nasal passages to airflow is about 60% of the resistance of the total air-conducting system. An adult then can drop the resistance of his airways considerably by breathing through his mouth. This mechanism is used for obtaining relief when lower airways are obstructed, and also during heavy exercise when a larger than normal amount of air must be turned over each minute and a lowered resistance can save energy. Infants, during the first two weeks of their lives, are obligatory nose breathers, except when they cry. This is due to the fact that their larynx stands high, their uvula almost touches the soft palate, their tongue is large and in their usual recumbent position obstructs the pharyngeal opening. Therefore, a young infant always breathes through its nose, even when the mouth is open. Perhaps as a small compensation for this disadvantage, the nasal resistance in infants is a relatively smaller portion, only about 40% of the whole airway resistance. Still it can only happen in this age group that total nasal obstruction, like in choanal atresia, can cause suffocation. It is rather remarkable that, regardless of their total reliance on nose breathing, newborns experience the same kind of periodic fluctuations in nasal resistance, due to an alternating congestion in the two nasal passages, as adults do. Again, as if balancing a handicap, there is evidence of a compensating mechanism by which babies decrease their lower airway resistance, probably in the glottis, when nasal resistance increases. This phenomenon may be specific to this age group.

Added to the above is another simple anatomical fact which probably means a disadvantage for the young child as compared to older people, when it comes to inflammation of the small airways. The bronchi are lined with ciliated columnar epithelium at every age. Perhaps the individual cells are a little shorter and wider in the infant, and more slender in the

older child. Still, there must be only a minimum difference between their actual size. However, they line air tubes with widely different internal diameters. Therefore when congestion or oedema enlarges these cells or the underlying tissue, the original cross-section area of the small baby bronchi must decrease much more than that of larger ones in older patients, and this evidently causes a disproportionate increase of airway resistance.

Histology of the bronchial walls reveals interesting age-related properties. One of them is the proportion of *smooth muscle* tissue in smaller and larger bronchi of children as compared to adults. In all age groups there is comparatively more muscle in the smaller than in the larger bronchi. However, in children's small bronchi there is less muscle than in the small bronchi of older people. In fact, during the first two years of life one may observe a distinct thickening of the muscular layer relative to the total cross-section of the wall in the small bronchi (Fig. 3a and b).

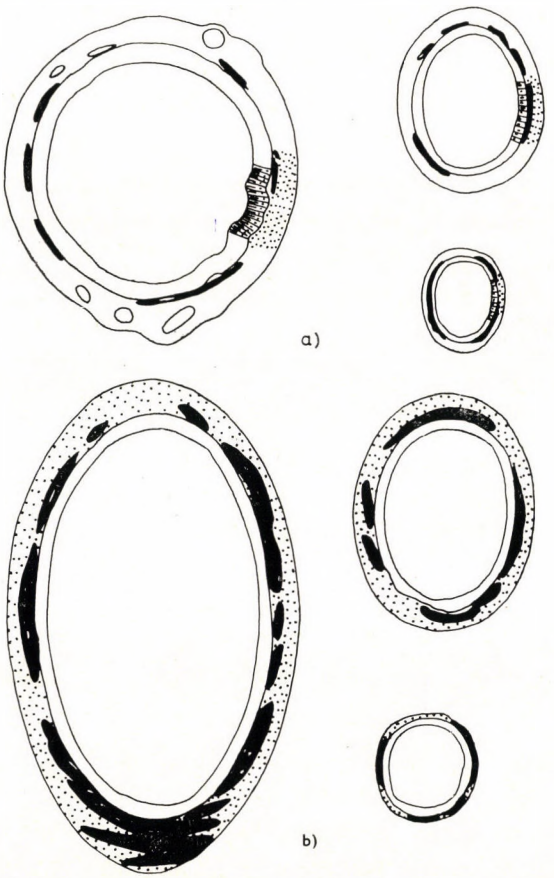

FIG. 3. a. Bronchioli from a newborn infant. Note the thin muscle; b. Bronchioli from a child aged 4 years. Note the relatively thick muscles. After Engel [4]

One may first think of the possibility that less muscle will produce less spasm. This may indeed be so. However, spasm is only one of the many factors causing pathological airway obstruction. Under normal conditions the role of muscles in this, like in any other, tubing system, is rather to maintain patency by their constant tone. A small bronchus which has no cartilage is the more collapsible the less rigid its wall; i.e., the less muscular tone there is contributing to wall rigidity. It can thus be assumed that under conditions of increased airway resistance, when expiratory positive pressure is applied, the small bronchi of young children have an increased tendency to collapse than those of older individuals.

Another phenomenon, somewhat related to the one just discussed, is the low total *static recoil pressure of the lung* in children as compared to young adults. The particularly interesting feature of this difference is that there is also a decline of this recoil force as one grows older which is very similar in magnitude to the one observed with decreasing age. A consequence of smaller recoil pressure is a smaller pull on the bronchi. This in turn allows airway closure or air trapping at a relatively larger lung volume, which then is a common property of the old and young, in contrast to young adults. It should be obvious that such conditions have more severe consequences of any airway obstruction in children, and also in old age. Fig. 4 shows the changes of static recoil pressure and "closing volume" with age.

An important anatomical component of the bronchial walls are *mucus glands and goblet cells*, which produce the mucus so importantly related to the physiological cleansing mechanism of the lungs. In any acute irritation or infection, and even more in chronic infections, a hyperplasia of these mucus producing organs occurs and airway obstruction is aggravated by an abnormal amount of secretion. It has been shown that the relative amount of mucus producing structures is larger in children than in adults. It follows then, that conditions which result in an overproduction of mucus will exaggerate the obstruction in

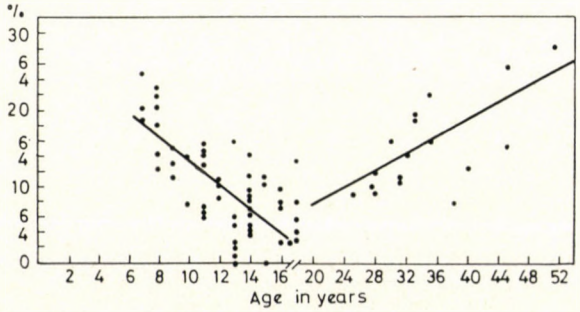

FIG. 4. "Closing Volume" as a percentage of vital capacity versus age. After Mansell et al. [9]

children as more mucus accumulates in smaller airways which already are handicapped by some of the other factors discussed above.

As to the structures and functions related to gas exchange, the *thickness of alveolar walls* is large in the newborn and gradually decreases during growth and development, so that the tissue to air volume ratio decreases with age. This may have an effect on the diffusion of gases across the alveolar-capillary barrier. It may not become significant until interstitial oedema or other pathologic factors aggravate the situation, but for this reason it must be taken into account. Oxygenation of arterial blood and CO_2 production are greatly dependent upon the *distribution of blood flow* throughout the lung, as well as on the distribution of ventilation. The blood vessels have a remarkable property of adaptation to regional hypoxia in the lung, in that they constrict when directly stimulated by low oxygen around them, so that the blood flow is diverted from the poorly ventilated areas to the better ventilated ones. This in effect restores, at least partially, the disturbed overall ratio of ventilation and perfusion and results in improved blood gas values. The *muscular layer of arteries* accompanying the airways, which is responsible for this adaptation mechanism, does not reach out as far into the periphery in infants and children as in adults. In fact, at birth there are no muscular arterioles at the acinar level and they reach, by gradual progression, the alveolar level only between 11 and 19 years of age. It seems then that infants and young children cannot compensate effectively for peripheral hypoxia by shunting away the blood flow. This assumption is borne out by the fact that small bronchopneumonic foci cause more severe hypoxia in young than in older patients.

Somewhat contradictory to the above observations is the fact that at a very early age there is, at some level of the pulmonary arterial system, a rather vigorous reaction to hypoxia which causes general hypoperfusion by vasoconstriction in foetal life, and again in severe hypoventilation such as in the respiratory distress syndrome, when most of the pulmonary blood flow is shunted through the still open or reopened intracardiac and ductal communications.

References

1. Avery, M. E.: The lung and its disorders in the newborn infant, 2nd ed., W. B. Saunders Co., Philadelphia 1968.
2. Dunnill, M. S.: Postnatal growth of the lung. Thorax **17,** 329 (1962).
3. Emery, J.: The anatomy of the developing lung. Heinemann, London 1969.
4. Engel, S.: Lung structure. Thomas, Springfield 1962.
5. Engel, S.: The prenatal lung. Pergamon Press, Oxford 1966.
6. Hislop, A., Reid, L.: Pulmonary arterial development during childhood: branching pattern and structure. Thorax **28,** 129 (1973).
7. Hogg, J. C., Williams, D. J., Richardson, J. B., Macklem, P. T., Thurlbeck, W. M.: Age as a factor in the distribution of lower airway disease, New Engl. J. Med. **282,** 1283 (1970).
8. Lacourt, G., Polgar, G.: Interaction between nasal and pulmonary resistance in newborn infants, J. appl. Physiol. **30,** 870 (1971).

9. Mansell, A., Bryan, C., Levison, H.: Airway closure in children. J. appl. Physiol. **33,** 711 (1972).
10. Martin, H. B.: The effect of aging on the alveolar pores of Kohn in the dog. Amer. Rev. resp. Dis. **88,** 773 (1963).
11. Matsuba, K., Thurlbeck, D.: A morphometric study of bronchial and bronchiolar walls in children, Amer. Rev. resp. Dis. **105,** 908 (1972).
12. Polgar, G.: Opposing forces to breathing in newborn infants. Biol. Neonat. **11,** 1 (1967).
13. Polgar, G.: Practical pulmonary physiology: a functional analysis of symptoms and therapeutic measures in respiratory disorders of newborn infants. Pediat. Clin. N. Amer. **20,** 303 (1973).
14. Woolcock, A. J., Macklem, P. T.: Mechanical factors influencing collateral ventilation in human, dog and pig lungs. J. appl. Physiol. **30,** 99 (1971).

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