Respiratory Physiology in the Newborn Infant

Mary Ellen Avery, M.D., and Colin Normand, B.M., M.R.C.P.†*

THE remarkable speed of adaptation from the placenta to the lung as the organ of gas exchange, and the efficiency of the respiratory apparatus of the newborn infant continue to awe those who ponder the adjustment. Moreover there is a significant balance between airway dimensions and alveolar surface area which changes with growth of the lung and the rest of the body. In the first days of life the respiratory quotient falls, body weight may fall about 10 per cent, and in the ensuing 5–6 months weight doubles. During this period changes in the circulation are underway as the fetal channels, foramen ovale and ductus arteriosus close, and pulmonary vascular resistance falls. It is difficult enough to comprehend the subtleties of ventilation-perfusion relations in the adult lung; their changing patterns during the cardiopulmonary adaptation at birth and shortly thereafter are even more complex.

The description of respiration in the newborn period requires measurements in the first minutes of life, followed by their repetition in a matter of hours and also days. A further requirement is methodology suitably miniaturized to permit examination of premature as well as term newborn infants. Lastly, limitations are imposed by the lack of active patient cooperation. Despite these problems, an abundance of descriptive information is available, most obtained in the past fifteen years (table 1).

Fetal Lung

The fetal lung contains fluid which is in part derived from the lung itself and in part may be aspirated amniotic fluid. The probability of a finite volume of fluid in the lung at birth was deduced by pathologists on the basis of observations of the distention of sequestered portions of lung[17] and occasional squamous cells from the fetal skin seen even in lungs of infants who died from non-pulmonary causes.[18] Studies of animal lungs show their greater weight in the fetal state compared with that after the initiation of respiration,[19, 20] and the lower specific gravity of fetal compared with gas-free newborn lung. Fluid can be seen flowing from the trachea of the exteriorized fetal animal[21, 22] and analysis of the fluid suggests it is an ultrafiltrate of fetal blood.[23] The volume of fluid normally present in the fetal lung is estimated at approximately one-half the functional residual capacity (FRC).[20] The rate of its disappearance is assumed to be very rapid on the basis of the establishment of gaseous FRC with the first breath[24] and the loss of lung weight within ten minutes of the initiation of respiration.

Postnatal Changes in Lung Volumes

The partition of lung volumes in the normal newborn infant is about the same as in the adult: Tidal volumes of 15–20 ml. are about 10 per cent of the total lung capacity, and the functional residual capacity of 75 ml. is 40–50 per cent of the total. Lung volumes bear a relationship to body size, as shown by Helliesen *et al.*[25] with the following regression equations from data obtained on infants, children, and adults.

Residual volume	$= 0.227 \times ht^{3.06} \times 10^{-3}$
Functional residual capacity	$= 0.598 \times ht^{3.00} \times 10^{-3}$
Vital capacity	$= 2.29 \times ht^{2.80} \times 10^{-3}$
Total lung capacity	$= 2.30 \times ht^{2.866} \times 10^{-3}$
Lung compliance	$= 0.713 \times ht^{2.836} \times 10^{-4}$
Flow resistance	= antilog $(1.954 - 0.0093 \times ht)$

* Associate Professor of Pediatrics, The Johns Hopkins University Medical School.
† Fellow in Pediatrics, The Johns Hopkins University Medical School.
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TABLE 1. Representative Values in Normal Infants at Term

	Umbilical vein	30 min.	1–4 hrs.	12–24 hrs.	24–48 hrs.	96 hrs.	Reference
		Arterial Blood					
pH	7.33		7.30	7.38	7.39	7.39	
P_{CO_2} mm. Hg	43		39	33	34	36	Reardon *et al.*[1]
HCO_3 mEq./liter	21.6		18.8	19.5	20	21.4	Oliver *et al.*[2]
P_{O_2} mm. Hg	28 ± 8		62 ± 13.8	68	63–87		Nelson *et al.*[3,4]
O_2 saturation			95%	94%	94%	96%	
Crying vital capacity ml. (for 3 kg. infant)		77 range (56–110)			92 (69–128)	100	Sutherland and Ratcliff[5]
Functional residual capacity, ml./kg.		22 ± 8	25 ± 8	21 ± 1	28 ± 7	39 ± 9	Klaus *et al.*[6]
Lung compliance ml./cm.H_2O/kg.		1.5 ± 0.05		2.0 ± 0.4		1.7	Cook *et al.*[7]
Lung compliance/FRC ml./cm.H_2O/ml.			0.04 ± 0.10	.053 ± 0.009		0.065	Chu *et al.*[8]
Right to left shunt as percentage cardiac output			22% (range 11–29%)	24% (17–32%)			Cook *et al.*[7] Prod'hom *et al.*[68]

		Comment	Reference
Respiratory frequency	34/min. range 20–60	1–2 days 1–11 days	Cook *et al.*[9] Cross[10]
Resistances cm. H_2O/liter/second	29, 26 18 ± 6.3	Total lung resistance Airway resistance	Cook *et al.*,[7] Swyer *et al.*,[11] Polgar[12]
Flow rates ml./second	a. 48 b. 37 161 106	Rest (a) Max. insp. Crying (b) Max. exp.	Swyer *et al.*,[11] Long and Hull[13]
Ventilation ml./kg./min.	200		Cook *et al.*,[9] Nelson *et al.*[3]
Dead space ml.	4.4–9.2	Term infants	Nelson *et al.*,[3] *Cook et al.*,[9] *Strang*[14]
Alveolar ventilation ml./kg./min.	120–145	First 3 days of life	Nelson *et al.*[3]
O_2 consumption ml./kg./min.	6.2	At neutral temperature	Oliver and Karlberg[15]
CO_2 production ml./kg./min.	5.1	At neutral temperature	Oliver and Karlberg[15]
Alveolar-arterial O_2 differences mm. Hg	28 ± 10, room air 311 ± 70, 100% O_2	Age 7 hrs. to 42 days Age 6 to 58 hrs. 3 infants	Nelson *et al.*[4]
Arterial-alveolar CO_2 differences mm. Hg	1.8 ± 3.8	Age 3 to 74 hours	Nelson *et al.*[16]

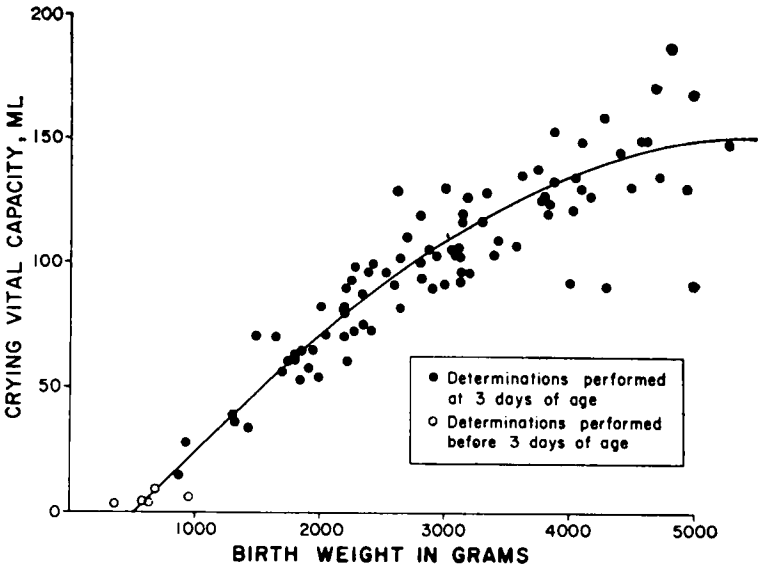

FIG. 1. The relation between "crying vital capacity" and birth weight in 93 infants. Determinations were performed on the third day of life except for a few infants under 1,000 g., indicated by open circles. (Reproduced with permission of Sutherland, J. M., and Ratcliff, J. W.: Amer. J. Dis. Child. 101: 67, 1961.)

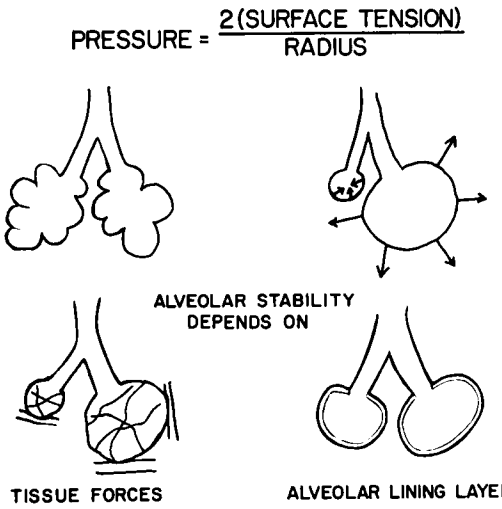

FIG. 2. Schematic illustration of how the La-Place relation, between pressure across a curved surface, surface tension at the air-liquid interface, and the radius of curvature of the surface, would promote an unstable equilibrium in the lung. Tissue forces, and particularly the alveolar lining layer, help to stabilize the air-spaces. (Reproduced with permission, Avery, M. E.: The Lung and Its Disorders in the Newborn Infant, Philadelphia, W. B. Saunders Co., 1964.)

The vital capacity of the infant cannot be measured in the same sense that it is in the adult, although an approximation to it can be made by measurement of the volume of a hard cry, the so-called crying vital capacity. Within 30 minutes of birth, a vigorous infant expires a volume of 56–110 ml. with a hard cry, which increases only slightly over the next few days.[5] The actual volume bears a relationship to body weight as shown in figure 1.

Several studies on functional residual capacity, measured serially, confirm the rapidity with which it is established in the normal infant. Some air remains in the lung after the first breath, as demonstrated roentgenographically and by reverse plethysmography.[26] Mean functional residual capacity before 10 minutes of age is between 15–20 ml./kg., from 11–20 minutes it is about 20–25 ml./kg., and by one hour, about 30 ml./kg.[6]

Lung Compliance

Changes in lung compliance occur with each breath after the first one; by 3 minutes of age, many infants have a lung compliance of 2 ml./cm. of water; by 60 minutes of age 4 ml./cm. of water is an average value, and there is very little change over the subsequent hours of life, although by one week a representative value is 5–6 ml./cm. of water.[26, 27]

It is important to relate lung compliance to a lung volume when both are changing. Since compliance denotes a property of the tissue, its stiffness if you will, a reduction in compliance infers an abnormality of the tissue. However, since volume is a part of the measurement, a low compliance could mean loss of volume or increased stiffness. This problem was circumvented by Chu *et al.*,[8] who reported lung compliance per functional residual capacity in a series of premature and term infants. When values of compliance are expressed per FRC, there is an increase in compliance in the early hours of life when there is no significant change in FRC. This observation suggests a change in tissue elasticity occurs during the early hours after transition from a fluid-containing to an aerated lung. Whether the change reflects alterations in interstitial water content, stress relaxation after the first few big stretches, or other geometrical changes is not clear. Previous studies of fluid-filling of fetal lungs compared to fluid-filling of airless adult lungs have shown differences which must reside in the tissue itself; the fetal lung tends to retain more fluid at atmospheric pressure than the adult lung.[20, 28]

The concept that emerges from these studies is that there are measurable differences in distensibility and volumes in the first hours and days of life, but the point of most significance is that the largest changes are in the first minutes of life, and those which continue over the ensuing days are of small magnitude.

Pulmonary Surfactant

A significant event in lung maturation occurs at about 1,000 g. weight in the majority of fetuses. About that time, alveolar cells become capable of producing a surface-active alveolar lining substance, or pulmonary surfactant.[31] This substance, the chief ingredient of the foam seen in pulmonary edema, is a lipoprotein containing dipalmitoyl lecithin. Its function is to confer stability on the terminal airspaces, or to act as an anti-atelectasis factor. Lungs which lack adequate amounts

of that material tend to collapse as smaller airspaces empty their contents into the larger ones.

The property of the lining layer or surfactant which makes the lung a stable emulsion of air in liquid is a capacity to change surface tension as surface area changes. Thus as the lung expands, surface tension is relatively high and the forces of surface tension add to the elastic recoil of the lung. As lung volume decreases, surface tension decreases, and the elastic recoil or tendency to collapse is reduced [29, 30] (fig. 2). If the pulmonary surfactant is not intact, either by failure to form in adequate amounts or by denaturation once produced, lungs are incapable of maintaining an adequate functional residual capacity of air. Each breath then resembles the first breath as moist airspaces must be re-opened by each subsequent breath. A deficiency of surfactant is found in lungs of immature animals and man, and in those who die from hyaline membrane disease.[31] The probability that atelectasis is present in life is based on radiographic findings of multiple small opacities, the reticulogranular appearance of the chest film with hilar consolidation, and on an early decrease in functional residual capacity in affected infants.[32] Experimentally the surfactant can be altered by pulmonary artery ligation in dogs, bronchial ligation,[33] respiratory acidosis in guinea pigs,[34] bilateral vagotomy

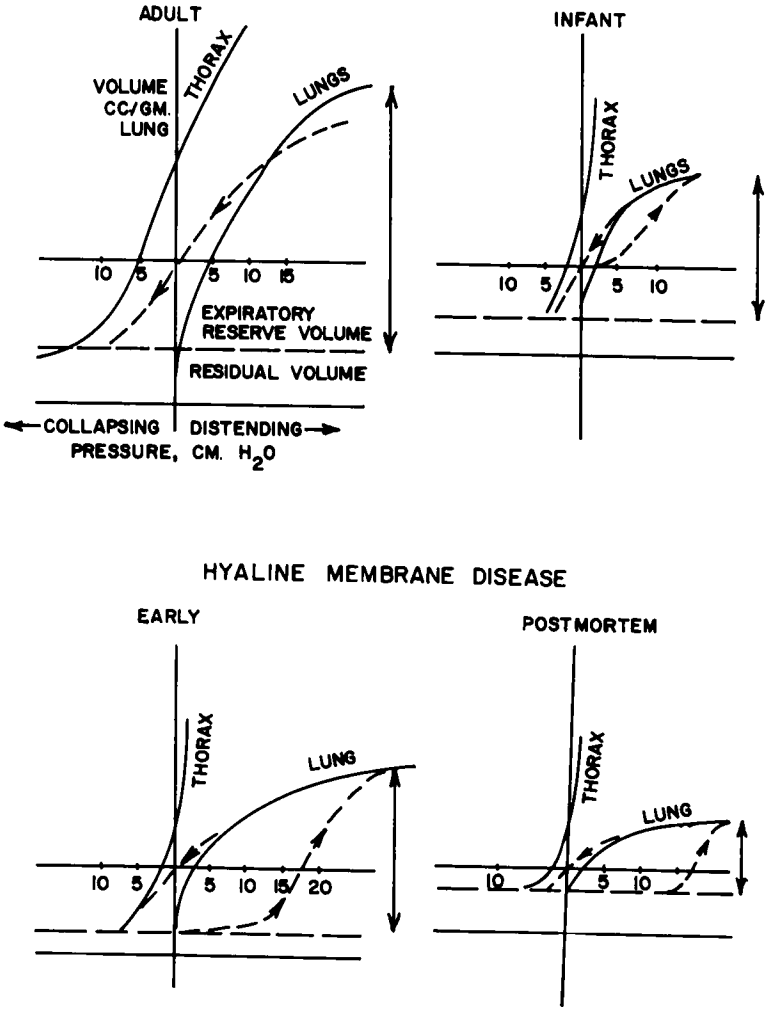

FIG. 3. Relaxation pressure-volume relationships of lungs and thorax, in infants and adults compared on the basis of lung weight. The dotted line represents lungs and thorax together. The thorax of the infant is more compliant than that of the adult; end-expiratory pleural pressures are lower in the infant. In hyaline membrane disease, the residual volume is decreased, lung compliance increased, and inflation pressures higher. (Reproduced with permission, Avery, M. E.: The Lung and Its Disorders in the Newborn Infant. Philadelphia, W. B. Saunders Co., 1964.)

in guinea pigs,[35] instillation of fluid and detergents into the lung,[36, 74, 75] and in pulmonary edema.[76] The role of similar pathologic events in the alteration of surfactant in man awaits further study.

Mechanical Properties of the Thorax

The compliance of the thorax is greater in younger individuals. This observation is obvious on inspection, since the older individual tends to have more rigid bones and a more barrel-like chest wall. The newborn infant has a less rigid bony structure, and the premature infant appears to have a nearly infinitely compliant thorax. When the lungs are abnormal and respiratory effort is marked, the sternum nearly approximates the vertebral column with deep inspiration to produce the pseudopectus deformity so commonly noted during respiratory distress.

Measurements of the compliance of the thorax in puppies, goats, and infants establish the greater change in volume per unit applied pressure in the younger of each species.[20, 37, 38]

One effect of the high compliance of the infant chest wall is that at the respiratory midposition, its elastic recoil is less than that of the adult. Thus the end-expiratory pleural pressure is only 1–2 cm. of water subatmospheric, in contrast to 3–5 cm. of water in the older age group[20] (fig. 3).

Dead Space

The value for the portion of each tidal volume which does not participate in gas exchange, or dead space, is to some extent a function of the way in which it is measured. If the dead space is calculated from carbon dioxide tensions in expired air and alveolar air it averages 4.4 ml. for term infants, or 30 per cent of a tidal volume.[3] If it is measured from tracings of end-tidal nitrogen after a period of oxygen breathing, it is closer to one-half of a tidal volume.[39] Apparently the dead space/tidal volume ratio is about the same in newborn infants as in adults. It is of some practical importance to note that a face mask with a dead space volume of only 5 ml. for an infant will be a dead space equivalent of 100–150 ml. for an adult.

Airway Resistance

The resistance to the flow of air through the airways depends on their size and numbers. Although the airways of the infant are smaller than those of the adult, they are not reduced proportionately to body size. Indeed, if they were, the first breath would have been impossible. Their numbers are reduced, according to the work of Dunnill[40] just as numbers of alveoli are reduced. Recent studies by Boyden and Tompsett[41] demonstrate the shallow shape of the alveoli, and that observation coupled with the finding of Loosli and Potter[58] of fewer elastic fibers in the newborn lung suggests the terminal ventilatory unit may be a saccule of larger dimensions than a single alveolus.

Respiratory resistance, measured from esophageal pressures and flow calculated from volume tracings, gives widely scattered values in normal infants, from 7 to 131 cm. of water/liter/second, with an average value of 29 cm. of water/liter/second.[7] Airway resistance, measured by a plethysmographic method, is lower, 18 cm. of water/liter/second on the average.[12] The contribution of the upper airway to total resistance is substantial. In one infant, nasal resistance measured by posterior rhinometry was 13.4 cm. of water/liter/second and the average by indirect measurement was 13 cm. of water/liter/second, or nearly half of total respiratory resistance,[42] as is the case in adults.[77]

Respiratory Frequencies

One of the striking observations in premature infants in particular, but also at term, is the variation in frequency and rhythmicity of respiration. An average frequency for the first days of life in term infants is 34 breaths per minute, but the range is from about 20 to 60 breaths per minute.[9] Hunger, temperature changes, and handling of the infant tend to increase the frequency. Presumably changes in lung compliance and airway resistance operate to alter frequency, although their quantitative effects are not well understood. Calculations of the work of breathing from pressure-volume tracings show a wide range of frequencies at which work is relatively low, with the minimal range at a frequency of 30–40 per minute.[7]

Similar studies in adults show a minimal work level at lower frequencies. Elastic work is greater at lower frequencies; flow resistive work increases at higher frequencies. It appears that both the infant and adult breathe at frequencies where there is a compromise between the two extremes. Since the studies of Mead [43] suggest that frequencies are selected where the average force applied by the respiratory muscles is least, it would be of interest to know if the infant too responds to a force signal for controlling frequency. Mead's observations suggest the lung is the principal if not the only site of receptors responsible for the frequency adjustment, and presumably vagal afferent nerves carry the information to the central mechanisms.

Periodic Breathing

Brief recurring periods of apnea in a sequence of breaths may be observed in almost all premature infants of less than 36 weeks gestational age, and rarely in term infants at sea level. This pattern, called periodic breathing, is more common in infants born at altitude than those at sea level [44] and thus may be accentuated by reduced inspired oxygen concentrations. It may occur in premature infants with normal arterial oxygen saturation, however, and thus appears to be related to the degree of maturation of central integrating mechanisms. The net effect of periodic breathing is mild hyperventilation, demonstrable by a slightly lower mean arterial carbon dioxide tension and a slightly higher mean pH in infants whose respiratory pattern is mostly periodic as compared with those with regular patterns.[45] There is no evidence that periodic breathing is harmful. The brief apneic periods (5 to 10 seconds) are not associated with significant bradycardia; the increase in the partial pressure of CO_2 is only 5 to 7 mm. of mercury.

Apneic Spells

Longer apneic intervals, associated with bradycardia and cyanosis are of most significance, and associated with a poor prognosis.[46] Increased concentrations of inspired oxygen do not always prevent such episodes; tactile stimuli such as turning the infant or slapping the feet seem to be the most effective means of restoring regular respiration.

Stimuli to Respiration

It is possible to demonstrate that chemical stimuli are effective in stimulating respiration in infants in whom normal breathing is once established. Studies of the ventilatory response to carbon dioxide establish that ventilation increases about two-fold with a 10 mm. of mercury rise in arterial P_{CO_2}. Infants at rest have lower CO_2 tensions than adults at rest, so the ventilation at a given P_{CO_2} is greater than that of the adult. The change in ventilation per mm. of mercury change in CO_2 tension is the same when ventilation is compared on the basis of body weight (fig. 4).[47]

The responsiveness of the chemoreceptors to oxygen has been demonstrated by the effect on ventilation of the administration of high concentrations of inspired oxygen. If there is a reflex drive while breathing the 20 per cent oxygen of room air, one would expect a decrease in ventilation on administration of 100 per cent oxygen. Brady *et al.* have shown a 10 per cent fall in ventilation within 2–6 seconds of reaching a $P_{A_{O_2}}$ of 170 mm. of mercury which lasted 20–60 seconds.[48] Thus chemoreceptor responsiveness to oxygen is present in the newborn infants as early as one hour of age. The effects of hypoxia appear to differ on the first day of life compared to 6–11 days of age. Miller and Behrle found a tendency toward hypoventilation in infants under 24 hours of age exposed to 12 per cent oxygen, whereas older infants had a transient hyperventilation.[49] The marked effect of environmental temperature on the ventilatory response of animals, pointed out by Hill, suggests that any conclusions about the responsiveness of infants should be based on studies in which temperatures are rigidly controlled.[50] Oliver and Karlberg [15] could not demonstrate a fall in oxygen consumption in infants breathing 15 per cent oxygen as long as they were warm. They did not measure transient changes in ventilation, however, nor did they compare the responses of infants less than 24 hours with older ones.

Nonchemical Stimuli

The recent work of Burns in the experimental animal has elucidated the role of "neuronal traffic" or nonchemical sensory input on the spontaneous discharges of the respiratory cen-

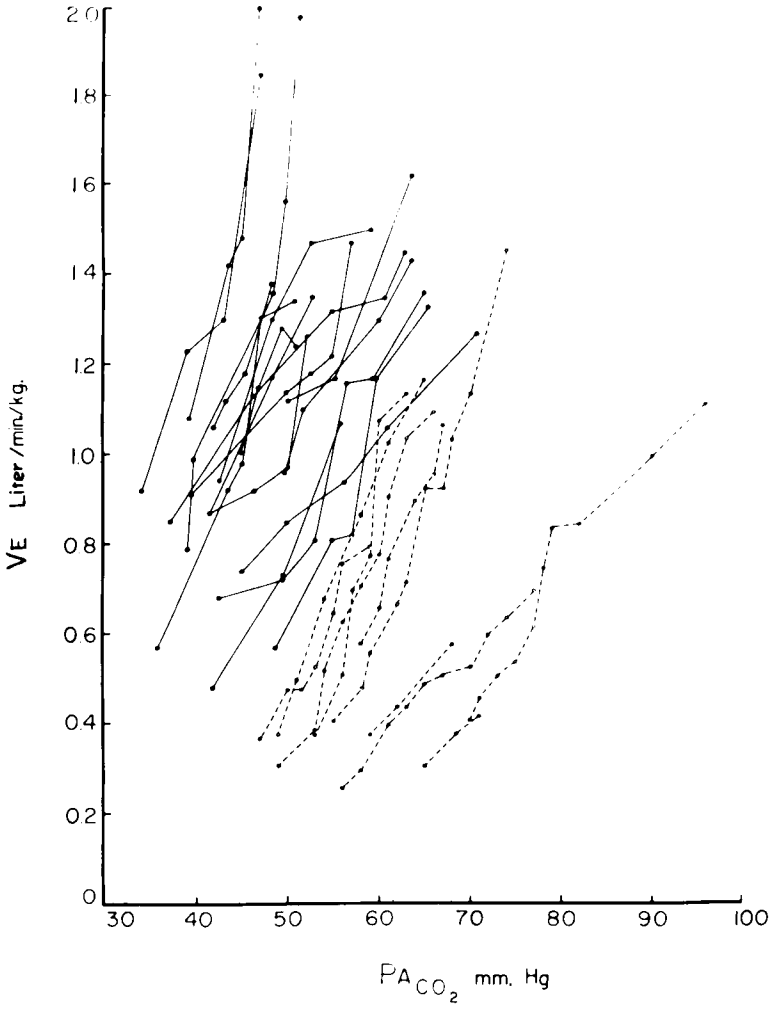

FIG. 4. The relation of ventilation per kilogram body weight to alveolar carbon dioxide tensions in infants (solid lines) and adults (dotted lines) measured by a rebreathing method. The mean slopes are the same. The displacement to the left of the infants is thought to be the combined effect of less buffer base, greater metabolism per kg., and tactile stimuli from application of a mask. (Reproduced with permission of Avery, M. E., and others: J. Appl. Physiol. **18**: 895, 1963.)

ter.[51] Stimulation of the cut end of the cervical cord resulted in an increase in the firing of the respiratory neurons as recorded by microelectrodes in the medulla. Clinical experience testifies to the role of the spanking in the initiation of respiration, or to the effect of cold water on the ventilation of the adult. The tactile stimuli given the apneic infant surely augment the discharges of the respiratory center.

The possibility that a change in the level of either chemical or nonchemical stimuli is significant in the control of respiration is attractive in that by analogy a changing stimulus evokes a larger response in other sensory systems. Small fluctuations in arterial CO_2 and O_2 tension occur in phase with respiration in air-breathing, since gas exchange is phasic in the lung. To what extent the chemoreceptors respond to the rate of change of gas tensions as well as their level is not established. Preliminary studies suggest that ventilation is greater at a given P_{CO_2} when inspired carbon dioxide is given intermittently compared with continuous administration.[52] Avery, Chernick and Young[53] found that the exteriorized fetal animal responded with a gasp when blood equilibrated with carbon dioxide was given as a bolus, and did not respond when the same blood was infused slowly. These studies suggest that the fetus may be less responsive to the level of CO_2 than to a sudden change, and this finding may in part contribute to the lack of sustained respiratory movements *in utero,*

and contribute to the rhythmicity of respiration when the lung becomes the organ of gas exchange.

Gas Exchange

The previous discussion has been concerned with the ventilation of the newborn infant. However, adequate respiration also involves the diffusion of gases across the alveolar membrane and appropriate perfusion with venous blood of ventilated alveoli. Table 1 shows that in the first few days of life arterial oxygen tensions are significantly below those found in older children and adults, indicating some degree of hypoxemia in spite of low P_{CO_2} levels which imply alveolar hyperventilation.

Measurements of diffusion capacity in the newborn are limited.[54, 55, 56] Stahlman using the steady-state CO method of Filley obtained an average figure in infants of 8.25 ml./minute/mm. of mercury/m.^{2} When compared on the basis of surface area, this falls within the range of 10.5 to 28.0, mean 17 ml./minute/mm. of mercury in adults.[57] Nelson measured the diffusion capacity for oxygen by using the Bohr integration procedure to determine mean capillary P_{O_2}, and low inspired O_2 concentrations to minimize venous admixture-like effects, and found values for DL_{O_2} of 5.5 ml./minute/mm. of mercury/m.^{2} or aboult half the equivalent figure for adults. However, considering the difficulties involved and the assumptions required to obtain these measurements in the newborn infant it is probable that they need not represent significant impairment of diffusion compared with the older subject.

Nelson *et al.*[16] have studied the ventilation/blood flow relationships of the newborn infant using careful expired gas sampling techniques and sampling umbilical arterial or arterialized capillary blood. Measurements of arterial-end tidal P_{CO_2} differences in 17 healthy newborn babies up to 4 days old showed these to be negligible indicating even ventilation-perfusion ratios throughout the lung. Furthermore, nitrogen equilibration data[4, 39] in expired gas have shown the remarkable evenness of pulmonary ventilation in the lung of the newborn more than an hour or two of age. In contrast, measurements of children ill with hyaline membrane disease show mean alveolar-arterial P_{CO_2} differences of 14 mm. of mercury, an estimated 50 per cent of alveoli functioning as physiological dead space, and considerable unevenness of ventilation.[16]

Alveolar-arterial P_{O_2} differences in healthy newborn infants over an hour of age were on the average, 28 mm. of mercury, approximately three times that found in adults. It has already been suggested that this difference cannot be accounted for by diffusion difficulties or abnormal ventilation-perfusion ratios, rather it is due to a true shunt on the basis of alveolar-arterial oxygen differences measured while the infants are breathing 100 per cent O_2. There is an average right-to-left shunt of 15 per cent of cardiac output in infants up to 4 days of age and much higher values were obtained for infants with respiratory distress.[4] In the first hour of life there are larger venous admixtures than can be accounted for by true right-to-left shunt, indicating that at this age there are also ventilation/perfusion abnormalities.[68]

The sites of the observed right-to-left shunt are not precisely known, but inferences may be drawn from studies of the pulmonary circulation of fetal and newborn animals, and some catheterization data on human infants. The appearance of the thick-walled pulmonary arteries and information about pressures and blood flow in the fetal lamb indicate that pulmonary vascular resistance is high with the major portion of right ventricular output passing through the ductus arteriosus.[59] There is a prompt fall in this resistance when the lungs are inflated with nitrogen but a much greater decrease in resistance occurs when the lungs are inflated with air.[62, 63] At the same time increasing oxygen tensions cause constriction of the ductus arteriosus *in vivo*[64] and in the isolated preparation.[67] This does not appear to be a complete closure immediately, however, and Dawes has emphasized the significance of the left-to-right shunt through the ductus arteriosus in the newborn animal. Although increasing left atrial pressures would tend to close the foramen ovale, persistent right-to-left shunt through this has been observed in lambs up to three days of age.[65]

In human infants bidirectional shunts through the ductus arteriosus have been observed up to six hours of age and left-to-right shunts up to 15 hours.[60, 69] In those cases where patency of the ductus has been demon-

strated, closure has taken place when the infants have been given 100 per cent oxygen to breathe with reopening when inspired oxygen concentration is lowered to 13 per cent.[66] Angiographic studies have shown a definite right-to-left shunt through the foramen ovale in newborn infants,[70] and this may be substantial in distressed babies.[65] James and Rowe have demonstrated reopening of these fetal channels with some right-to-left shunt in infants up to 11 days of age given 10 per cent oxygen to breathe for short periods.[71]

Transition from the fetal circulation then appears to be largely dependent on the increased oxygen environment of the lungs, but for a few days after birth regression to the fetal status can occur with hypoxic and perhaps other stimuli.

Clinical Comment

One might well ask what are the oustanding features of the lung of the newborn infant which distinguish it from the adult lung, and what must be kept in mind during assisted ventilation of the infant.

Of first importance is some notion of the magnitude of volumes and pressures tolerated by the infant. A tidal volume of 15 to 20 ml. at a frequency of 30–40/minute should be adequate in the term infant. The least possible amount of dead space in equipment is appropriate, since the infant's own dead space is 5 to 9 ml. The infant develops the same changes in pleural pressure during quiet breathing as the adult, and the excised lung tolerates the same pressures at peak inflation, 30 to 35 cm. of water. Thus the infant's lung is not more fragile than that of the adult. If anything, the larger ratio of stroma to potential airspace in the infant may make it "tougher."

Blood gases in the normal infant are about the same as in the adult. An arterial *p*H of 7.40 is normal. Bicarbonate levels are somewhat lower in the first days of life, and the P_{CO_2} is closer to 35 mm. of mercury than the 40 mm. of mercury in the resting adult. The larger right-to-left shunt in the first days of life result in a slightly lower P_{O_2}, but the arterial oxygen saturation is 90 per cent or greater.

The metabolism per kilogram body weight in the infant is about double that of the adult; lung surface area per unit body weight is estimated to be about the same, thus the infant has less reserve lung surface area to meet added metabolic requirements. A cool environment for the infant results in larger heat losses because of the large surface to volume ratio, and is metabolically costly in that oxygen consumption may double or triple over resting values in a warm or thermally neutral environment. Thus the added effects of cooling, activity, and any pulmonary dysfunction may precipitate respiratory failure with carbon dioxide retention and hypoxia.

Fears about the use of high inspired oxygen mixtures have been based on the finding of retrolental fibroplasia in premature infants given more than 40 per cent oxygen. In this regard, the dangers of over-oxygenation of the infant remain as great as ever. However, the fact that retrolental fibroplasia results from high oxygen tensions in the blood has been occasionally ignored. An infant who remains cyanotic even in the presence of 100 per cent oxygen is not subject to the risk of retrolental fibroplasia, but he faces the risk of death from hypoxia.[72] The tolerance of the newborn lung to high oxygen tensions would seem to exceed that of the adult animal, since it was the experience of investigators who tried to produce retrolental fibroplasia by exposing animals to pure oxygen for several days, that the adult animals had to be removed from the oxygen environment for pulmonary reasons long before the young animals.[73] Thus judicious oxygen therapy is important, with no arbitrary upper limit in terms of the environment, but rather the goal is to achieve optimal concentrations in the blood regardless of the inspired concentration.

Support of the circulation is essential in effective assisted respiration in the infant, just as in the adult. Conditions in which assisted ventilation is indicated are often associated with peripheral vascular collapse, and artificial respiration tends to further impede venous return to the heart. However, there is minimal experience with the use of vasopressor agents in the infant; transfusions can be used although circulatory overload is a danger. Methods to maintain arterial blood presssure at normal systolic levels of 50 to 70 mm. of

mercury and to promote venous return during assisted breathing, need to be evaluated.

Finally, there is no way to prescribe a set of directions which will be applicable to every infant who needs ventilatory assistance. Serial measurements of carbon dioxide tension are essential guides to the optimal adjustment of a respirator, and if increased concentrations of inspired oxygen are used, arterial oxygen tensions are helpful to avoid excessive oxygen levels which could cause retrolental fibroplasia. The changing state of the lungs and the circulation in the first hours of life demand changes in the setting of any instrument currently available. The experienced and knowledgeable physician determines the success of artificial respiration.

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The embryo sits, according to medieval (and Renaissance) belief, in an eggshaped uterus, facing the mother's back. Just before birth, the baby was supposed to turn toward the maternal navel.