The Intensive Care of the Newly Born

Physiological Principles and Practice

Paul R. Swyer, Toronto, Ontario
With a contribution by M. Ann Llewellyn, Toronto, Ontario

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Foreword

During the past few years we have been faced with the seeming paradox of a decreasing birth rate, due to a cry for family planning, population control and abortions on demand, and an equally loud cry for intensified efforts to prevent prematurity, produce normal babies, and save seriously ill newborn infants suffering from a variety of congenital and acquired conditions.

This has resulted in the development of a new discipline – perinatology, with study of the reproductive process from the time of conception through delivery and the first month of neonatal life.

Although this book is directed mainly at the provision of intensive care for the seriously ill newborn, the author and all who contributed to it are staunch proponents of prevention and have pioneered the concept of regionalization of perinatal care, constant monitoring of the events of pregnancy and development of high risk units.

Neonatal intensive care is expensive and time-consuming and requires costly equipment and facilities, but above all, specially trained and dedicated personnel, be they physicians, nurses or technologists. The question is often asked: 'Is it worthwhile?'

In the epilogue, Dr. *Swyer* states: 'Careful data collection and follow-up studies indicate that despite the numerically increased survival of risk infants, both the relative proportion and absolute numbers of brain-damaged individuals are decreasing and there are prospects that up to 50 % of the diseases causing long-term institutionalisation are preventable by the full application of present knowledge of reproductive medicine, including neonatal intensive care.'

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Preface

This manual has been assembled primarily as a guide for physicians to a physiologically directed intensive care of the seriously ill newborn.

Intensive care, particularly in the newborn, is a rapidly developing and changing field. Commission to paper involves the risk of instant obsolescence. However, a body of practice based on physiological and biochemical principles is emerging and this manual represents an attempt to set it down for the guidance of physicians at all levels and ultimately for the benefit of their patients. Administration and organisation of neonatal intensive care are included.

I am particularly grateful to generations of fellows and residents who have taught me rather than the converse. Dr. *Ann Llewellyn* has contributed an important practical section on ventilatory techniques. Many staff members have helped with their advice amongst whom I would particularly acknowledge Drs. *C.S. Anglin, M. Braudo, A.C. Bryan, M. Heather Bryan, J.D. Burrington, G.W. Chance, S. Ein, R. Farber, P. Fleming, D. Fraser, J.R. Hamilton, W.B. Hanley, T.M. Hunt, B.S.L. Kidd, H. Levison, P.D. McClure, P.J. Middleton, C. Netley, Margaret G. Norman, J.B. Owen-Thomas, Ingeborg C. Radde, R.D. Rowe, A. Sass-Kortsak, S. Segal* and *P. Wei.* This list is not exhaustive and could easily include the whole staff of the hospital who are involved in neonatal care and with whom helpful discussion has taken place. I wish to acknowledge the indispensable help of my secretary, Miss *P. Taggett* in preparing the manuscript.

I am particularly grateful to Professor *H.W. Bain* for his encouragement and support for the Division of Perinatal Medicine's efforts to develop Intensive Care in the Hospital for Sick Children, Toronto.

August, 1974

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Prologue – in the Beginning

At delivery the fetus undergoes the most profound physiological stress he will ever again be called upon to withstand. The placenta's gas exchange function is replaced by a lung, its nutritive function by the alimentary tract, and its excretory function by the kidneys.

The pulmonary by-passing fetal shunts (ductus arteriosus and foramen ovale) functionally close within a few hours of birth. The central nervous system is stimulated by proprioreceptive and exteroreceptive messages and begins to exercise control of the internal environment. Premature or abnormal delivery, fetal disease such as rhesus blood group incompatibility or placental insufficiency, and intercurrent neonatal disease, lead to impairment of these control mechanisms indicating the *need for intensive care.* External control of the environment is demanded together with detection and correction of deviations in the newborn's internal environment.

The physiological concerns of intensive care of the newborn are:

(1) cardiopulmonary function and oxygenation,

(2) energy metabolism, nutrition and thermoregulation,

(3) acid base balance,

(4) fluid and electrolytic homeostasis.

Part I, chapters 1–5 will deal with these general physiological principles in the context of neonatal intensive care. Part II, chapters 6–10 are concerned with the evaluation and management of the seriously ill newborn from the moment of birth, including the organisational aspects. Part III, chapters 11–20 deal with the care of specific neonatal conditions. The Epilogue discusses outcome, evaluation, cost and cost effectiveness of intensive care.

Chapter 1

Cardiopulmonary System and Oxygenation

I. Respiration

Prior to delivery the lungs contain about 30 ml/kg of fluid which is a modified plasma ultrafiltrate. During vaginal delivery, the thorax is compressed by pressures of up to 70 cm H_2O forcing more than half of the pulmonary fluid up the tracheobronchial tree to the exterior (1). As the thorax is delivered, the elastic rib cage recoils and some of the ejected fluid is replaced by air, a process aided by glossopharyngeal movements which can force 8–10 ml of air into the trachea. Up to one third of the fluid remains in the lungs and may cause transient tachypnoea or pulmonary oedema in the first 24 h of life if absorption is delayed (p. 129). The amount remaining may be relatively greater following Caesarean section delivery because of the lack of chest compression.

A. First Breath

The resistances to spontaneous or artificial lung inflation are: (1) lung parenchymal (surface tension) resistance, dependent on the mutual adhesion of the unexpanded alveolar walls contributing more than 80 % of the total initial resistance to inspiration; (2) elastic resistance of the tissue contributes $>$ 10–15 % of the remainder, and (3) viscous resistance, which includes lung tissue deformation and airflow components and contributing less than 5 % of the total.

The stimulus to the first breath is probably a composite of chemoreceptive, lung, joint and muscle proprioceptive, thermal and surface sensory stimuli to the respiratory area of the mid-brain. There is interdependence between PaO_2 and $PaCO_2$ chemostimulation to the first breath (fig. 1). Thus initiation of ventilation is provoked by a low PaO_2 but the effectiveness of each stimulus is potentiated by an inverse relationship with the other (2). The respiratory centre may be depressed by asphyxia or maternal anaesthesia. Continued unresponsiveness to moderate skin stimulation indicates more profound depression and the urgent need for artificial inflation of the lungs, following suction clearance of the airways of mucus, blood, meconium or fluid.

Subatmospheric pressures of 30–80 cm H_2O (usually $\sim$35) are developed in the pleural space with the first breaths but since the duration of these high

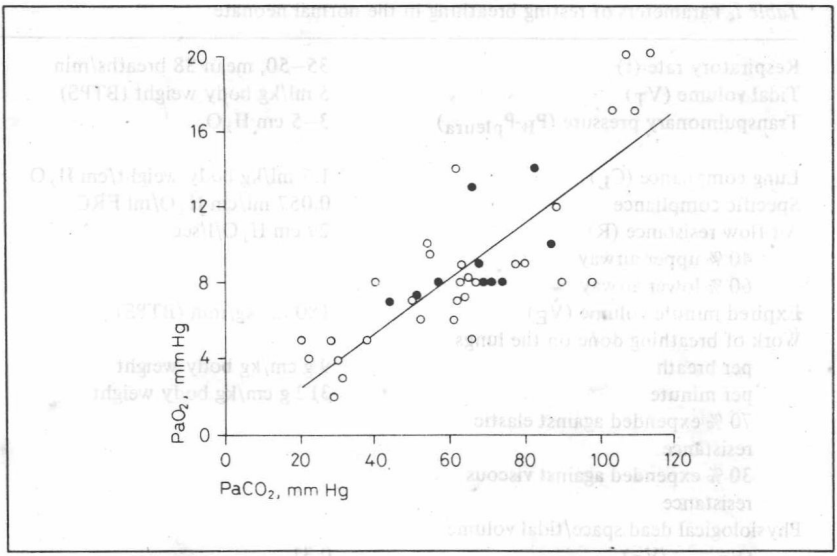

Fig. 1. The relation between PaO_2 and $PaCO_2$ at the time of the first breath in newborn lambs. ○ = Cross-circulation, ● = cord occlusion. Reproduced by permission of Dr. *V. Chernick* and the *Journal of Applied Physiology* (2).

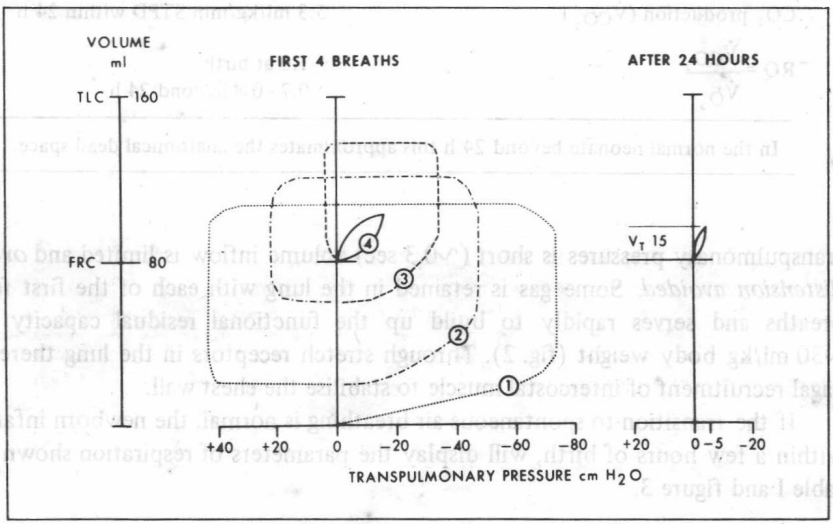

Fig. 2. Idealised diagram of the first four breaths of a newborn. Tidal air changes are plotted against intra-oesophageal (intrapleural) pressure change. Note the large transpulmonary pressures, subatmospheric in inspiration and supra-atmospheric in expiration, with the first breaths. Note also the retention of a significant volume at the end of the breaths. Based on data of the author and from *Karlberg* (1).

Table I. Parameters of resting breathing in the normal neonate

Respiratory rate (f)	35–50, mean 38 breaths/min
Tidal volume (V_T)	5 ml/kg body weight (BTPS)
Transpulmonary pressure (P_B-P_{pleura})	3–5 cm H_2O
Lung compliance (C_L)	1.7 ml/kg body weight/cm H_2O
Specific compliance	0.057 ml/cm H_2O/ml FRC
Air flow resistance (R)	29 cm H_2O/l/sec
40 % upper airway	
60 % lower airway	
Expired minute volume ($\dot{V}_E$)	180 ml/kg/min (BTPS)
Work of breathing done on the lungs	
per breath	9 g cm/kg body weight
per minute	312 g cm/kg body weight
70 % expended against elastic resistance	
30 % expended against viscous resistance	
Physiological dead space/tidal volume ($V_{D_{phys}}/V_T$)	0.31
Alveolar ventilation ($\dot{V}_A$)	125 ml/kg BTPS
Oxygen uptake ($\dot{V}_{O_2}$)	5.3 ml/kg/min STPD within 24 h
CO_2 production ($\dot{V}_{CO_2}$)	5.3 ml/kg/min STPD within 24 h
$RQ = \frac{\dot{V}_{CO_2}}{\dot{V}_{O_2}}$	∼1.0 at birth ∼0.7–0.8 beyond 24 h

[1] In the normal neonate beyond 24 h this approximates the anatomical dead space.

transpulmonary pressures is short (∼0.3 sec) volume inflow is limited and *over-distension avoided.* Some gas is retained in the lung with each of the first few breaths and serves rapidly to build up the functional residual capacity to ∼30 ml/kg body weight (fig. 2). Through stretch receptors in the lung there is vagal recruitment of intercostal muscle to stabilise the chest wall.

If the transition to spontaneous air breathing is normal, the newborn infant, within a few hours of birth, will display the parameters of respiration shown in table I and figure 3.

B. Surfactant

With each succeeding breath preformed lung surfactant coats the alveolar walls, alveolar surface tension is lowered and less pressure is required to open alveoli; less tidal air is retained at the end of each breath as the functional

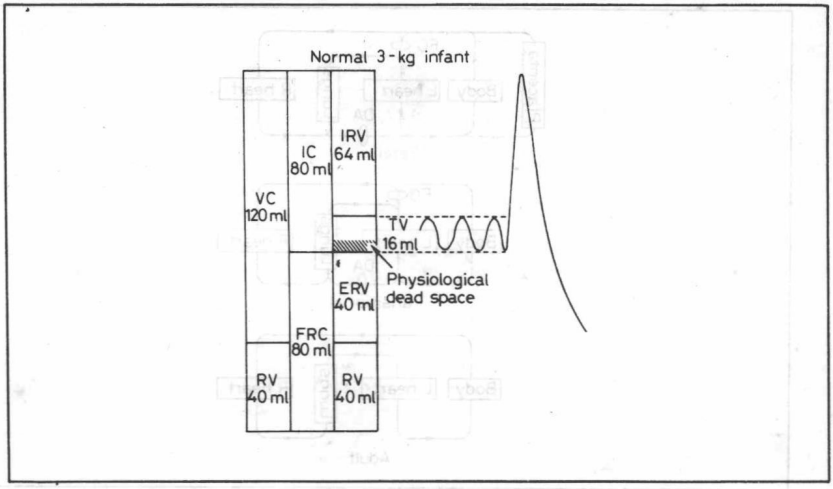

Fig. 3. Volumetric subdivisions of the lung of a normal newborn infant. VC = Vital capacity, RV = residual volume, IC = inspiratory capacity, FRC = functional residual capacity, IRV = inspiratory reserve volume, TV = tidal volume, ERV = expiratory reserve volume.

residual capacity is built up. Tidal volume lessens from the initial 30–80 ml to that appropriate to the baby's size (~5 ml/kg) (fig. 2). In addition surface tension lowering surfactant ensures the stability of the alveoli during expiration by preventing end-expiratory alveolar closure.

Surfactant has been detected in the lungs of the human fetus between the fifth and sixth gestational months, but is relatively deficient until term is approached and its formation is impaired by perinatal asphyxia (p. 104). Surfactant deficiency is the basic defect underlying the progressive atelectasis of the respiratory distress syndrome (RDS) in which small airway and air sac closure correlate with reduced or absent lung surfactant during the first 48–72 h of life (3). Prompt and efficient lung expansion and the correction of the biochemical consequences of asphyxia at birth are clearly vitally important.

II. Circulatory Changes at Birth

A. Prior to Delivery

Only 10 % of right ventricular output flows through the lungs, and most of the inferior vena caval inflow to the right atrium is diverted by the crista terminalis to the left atrium and distributed systemically. The majority of pulmonary flow by-passes the lungs through the ductus arteriosus to the descending aorta. With the first breath, geometric changes in the lung vasculature, increasing

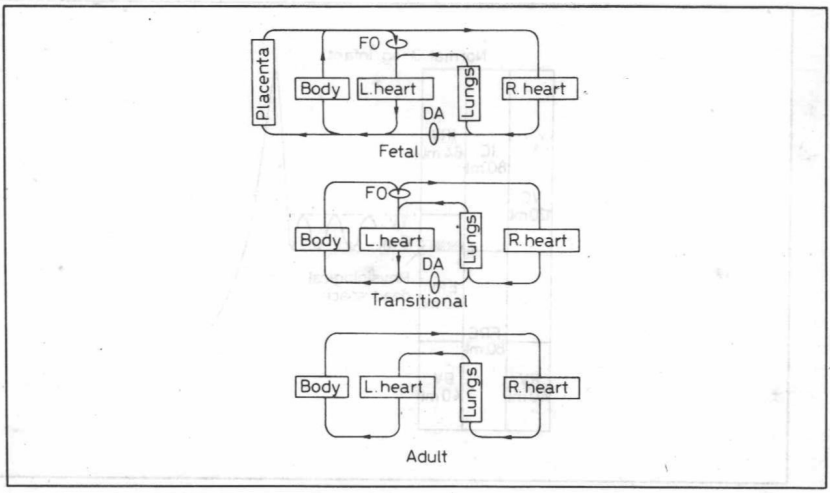

Fig. 4. Changes in the circulation after birth. Reproduced by permission of Dr. *G.S. Dawes* and Year Book Medical Publishers, Chicago (22).

PaO_2, decreasing $PaCO_2$, and rising pH produce a rapid drop in the pulmonary vascular resistance (4). Pulmonary blood flow increases, exposing more blood to gas exchange. The increased venous return from the lungs raises left atrial pressure, closing the foramen ovale. Right atrial blood is then directed to the right ventricle and lungs. This represents the transitional circulation (fig. 4). Contact of the ductal walls with blood of increasing oxygen tension stimulates contraction of smooth muscle in its wall producing ductal constriction. Whereas blood pressure in the pulmonary artery and aorta with the ductus widely patent are at first equal, combined ductal narrowing and lowered pulmonary vascular resistance result in a ductal pressure gradient, so that predominant ductal flow, while phasic and bidirectional, is towards rather than away from the lungs during the second hour of life. Finally there is functional and later anatomical closure of both ductus and foramen ovale and the normal 'adult' separation of pulmonary and systemic circulation is accomplished (fig. 4).

Circulating blood volume. Although late clamping of the umbilical cord can increase blood volume by ∿30 ml/kg, this leads to a significant increase in heart size and a fall in lung compliance. Subsequently blood volume is reduced to 90 ml/kg body weight in the first 12 h of life by loss of fluid, electrolytes and plasma proteins (5) to the interstitial space and sequestration in the spleen.

B. At Birth

Increased pulmonary blood flow must take place and although blood gas tensions and hydrogen ion concentration must change appropriately for effective

pulmonary vasodilation, bradykinin release from inactive precursors into the pulmonary circulation is also concerned (6). Lowering of temperature and pH in umbilical venous blood at delivery triggers its release.

C. Following Birth

In the hours following birth, the infant has an increased pulmonary blood flow in relation to ventilation. Additionally, 'physiological' right-to-left shunts of up to 20 % of the cardiac output (via foramen ovale and ductus arteriosus) result in A-a gradients for P_{O_2} of 20–40 mm Hg while breathing room air, increasing to over 300 mm Hg on breathing ∿100 % oxygen (7). At increased inspired oxygen concentrations every 1 % of cardiac output shunted R → L provides enough desaturated haemoglobin to combine with dissolved O_2 so that PaO_2 is reduced by ∿15 mm Hg (8). Below a PaO_2 of 130 mm Hg, this rule does not apply because the relationship between oxygen tension and saturation becomes alinear (fig. 5). In the first 24 h of life and to a diminishing extent afterwards, the PaO_2 in the normal newborn is substantially below that of the

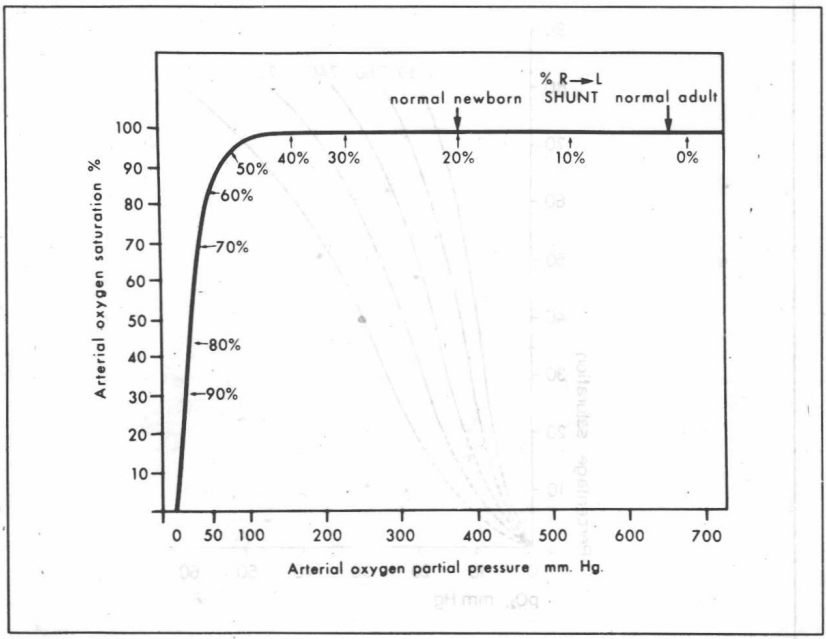

Fig. 5. Oxygen saturation/tension curve (extended for 100 % oxygen breathing) showing effects of various volumes of venous admixture. Down to arterial oxygen tension of ∿130 mm Hg, each 1 % of venous admixture reduces arterial oxygen tension by ∿15 mm Hg (8). Below 130 mm Hg the relationship becomes alinear and the rough rule no longer applies. Reproduced with permission of the author and publishers (23).

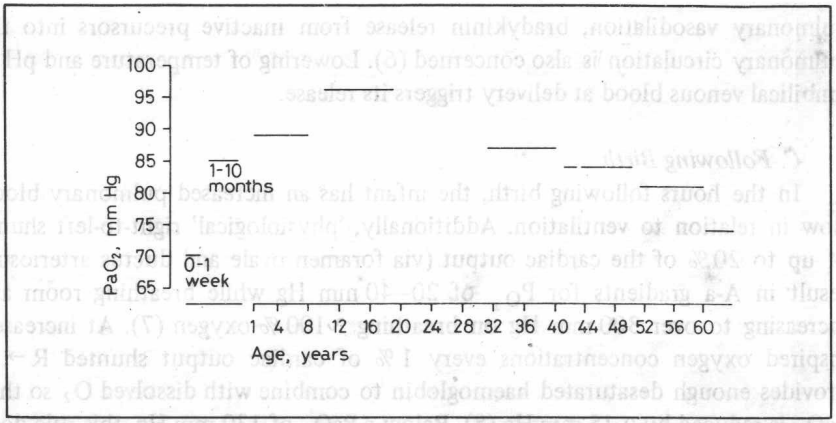

Fig. 6. Oxygen tensions in the newborn and at various subsequent ages. Data of *Mansell et al.*, (18) and *Sorbini et al.* (24).

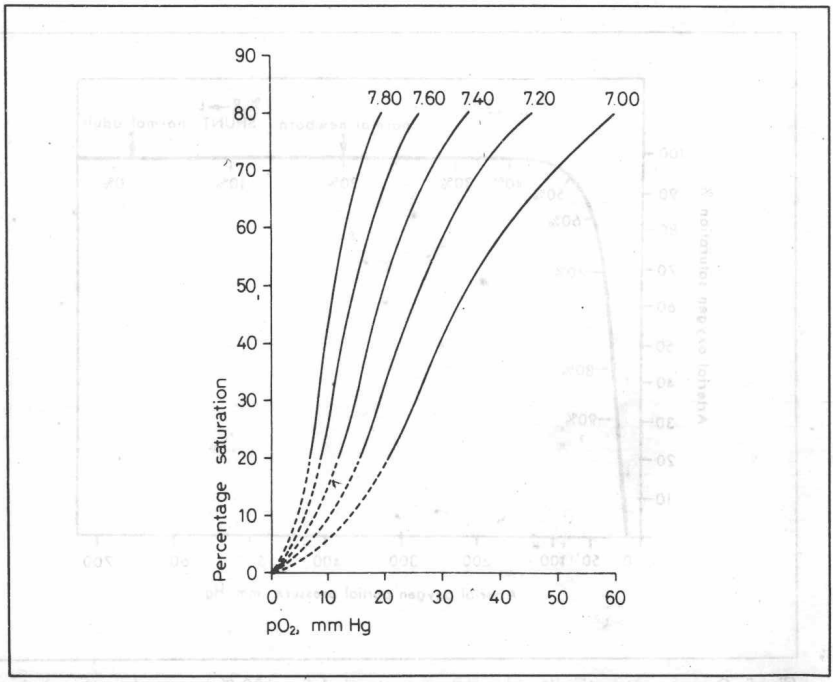

Fig. 7. Oxygen-haemoglobin dissociation curves for fetal blood at various pH levels. Note that acidaemic blood is less saturated at a given oxygen tension than blood of a normal pH. Reproduced by permission of Dr. *A.E. Hellegers* and the *American Journal of Obstetrics and Gynaecology* (9).

adult (fig. 6). However, neonatal blood contains 80 % fetal haemoglobin with a saturation/tension curve shifted to the left so that at PaO_2 >50 mm Hg arterial blood is fully saturated with oxygen (cf. >90 mm Hg for the adult). The acidaemic neonate's saturation/tension curve shifts back to the right, and for a PaO_2 of 50 mm Hg has an arterial oxygen saturation of 75 % at pH 7. Cells containing fetal haemoglobin carry more oxygen as oxyhaemoglobin at a given PaO_2 than cells containing adult haemoglobin or acidaemic blood cells (fig. 7) (9). This effect is probably related to cellular content of 2,3-diphosphoglycerate (2,3-DPG) (p. 12).

III. Implications for Intensive Care at Birth

(1) The lungs should be fully expanded as soon as possible after birth, artificially if necessary, since this initiates the sequence of adjustments leading to normal ventilation and perfusion, thus promoting normal gas exchange and functional separation of the pulmonary and systemic circulations.

(2) The relation between alveolar oxygen tension and arterial oxygen tension can be used to calculate the proportion of the cardiac output which is shunted from right to left (i.e. the total venous admixture) (Appendix II).

(3) Acidaemia impairs the oxygen carrying capacity of the blood. On the other hand, alkalaemia may impair off loading of oxygen at the lower oxygen tension in the tissues by rendering the red cell more retentive of oxygen at these tensions. A normal pH most effectively aids tissue oxygenation.

(4) The neonatal circulation is in a highly labile state and can revert within seconds or minutes to the fetal pattern under the influence of hypoxaemia, hypercapnoea, acidaemia or catecholamine release, all of which promote pulmonary vasoconstriction. The fetal type of circulation is entirely inappropriate for air breathing and, if uncorrected, is fatal.

The implications for postnatal intensive care are obvious: (i) prime attention to ensuring oxygenation and alveolar ventilation; (ii) treatment of acidaemia and support of the circulation by external cardiac massage (p. 62) and transfusion. The application of these measures requires early detection of abnormalities by close observation and continuous monitoring.

IV. Postnatal Respiration

The maintenance of rhythmic respiration in neonates is dependent on vagal reflexes and in this respect they are unlike adults. *Hering and Breuer* (10) in 1868 showed that animals had pulmonary stretch receptors which, when the lung was inflated, terminated the inspiratory effort. This reflex was vagally

mediated and was subsequently demonstrated in many animal species. These reflexes are weak or absent in adult man (11, 12), but *Cross et al.* (13) showed that they were present in full-term neonates for the first 100 h after birth. These reflexes are also present and persist in premature infants for many months (14). The function of these reflexes in the neonate is still unclear, however, the following suggestions have been advanced.

(1) The Hering-Breuer inflation reflex represents a simple rhythm generator at a time when other parts of the respiratory control system may not be fully mature.

(2) The inflation reflex, by limiting tidal volume, increases respiratory rate. This is the reason that the respiratory rate of newborn infants is so high. At a high respiratory rate, as expiratory time is short, the end-expiratory lung volume rises. This may be an important mechanism for keeping the lung expanded after birth.

(3) These reflexes have been shown to increase the stability of the chest wall (15). The stretch receptors sense respiratory loads (i.e. nasal obstruction) and there is immediate recruitment of intercostal muscles to maintain the tidal volume. In neonates this reflex is powerful, nearly tripling the stiffness of the thorax, and is probably very important in the first breath and other mechanical respiratory loads.

For efficient gas exchange there must also be proportionate contact between gas and blood, the correct gas flow/blood flow ratio must be established. In physiological terms this is the alveolar ventilation/perfusion ($\dot{V}_A/\dot{Q}_c$) ratio for the lung.

Little is known about the regional matching of ventilation to perfusion in the infant lung, partly because the bi-directional and multi-level anatomical shunts make studies difficult. However, there are some general principles. Most of the $\dot{V}_A/\dot{Q}_c$ variance in the adult is due to a gravitational gradient of perfusion, because the pulmonary artery pressure is low and the lung is large. Perfusion in the neonate, however, must be practically uniform, because the pulmonary artery pressure is high after birth and the lung is small. The distribution of ventilation is harder to predict. In adults the distribution is dependent on the regional compliance, which is determined by regional alveolar size which depends on the gradient of pleural pressure. Because the neonate's lung is small one would predict that regional pleural pressure differences would be small. However, *Agostini and D'Angelo* (16) have shown that the smaller the animal, the larger is the pleural pressure gradient. If this applies to infants, they will have the same differences in pleural pressure as adults and hence the same differences in regional alveolar size, and ventilation as adults. A further difficulty is that the peripheral airways resistance in neonates is very high (17) unlike the adult and it is possible that regional resistances play a significant role in ventilation distribution. The final problem is the question of airways closure. It has been shown in