Neonatal Anaesthesia and Perioperative Care

Second Edition

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Current Topics in Anaesthesia

General Editors: Stanley A. Feldman
Cyril F. Scurr

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Neonatal Anaesthesia and Perioperative Care

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General preface to series

The current rate of increase of scientific knowledge is such that it is recognized that '... ninety per cent of all the existing knowledge which can be drawn upon for the practice of medicine is less than 10 years old'.*

In an acute specialty, such as anaesthesia, failure to keep abreast of advances can seriously affect the standard of patient care. The need for continuing education is widely recognized and indeed it is mandatory in some countries.

However, due to the flood of new knowledge which grows in an exponential fashion greatly multiplying the pool of information every decade, the difficulty which presents itself is that of selecting and retrieving the information of immediate value and clinical relevance. This series has been produced in an effort to overcome this dilemma.

By producing a number of authoritative reviews the Current Topics Series has allowed the General Editors to select those in which it is felt there is a particular need for a digest of the large amount of literature, or for a clear statement of the relevance of new information.

By presenting these books in a concise form it should be possible to publish these reviews quickly. Careful selection of authors allows the presentation of mature clinical judgement on the relative importance of this new information.

The information will be clearly presented and, by emphasizing only key references and by avoiding an excess of specialist jargon, the books will, it is hoped, prove to be useful and succinct.

It has been our intention to avoid the difficulties of the large textbooks, with their inevitable prolonged gestation period, and to produce books with a wider appeal than the comprehensive, detailed, and highly specialized monographs. By this means we hope that the Current Topics in Anaesthesia Series will make a valuable contribution by meeting the demands of continuing education in anaesthesia.

Westminster Hospital
London

Stanley A. Feldman
Cyril F. Scurr

* Education and Training for the Professions.
Sir Frank Hartley, Wilkinson Lecture
Delivered at Institute of Dental Surgery, 30.1.78
University of London Bulletin, May 1978, No. 45, p. 3

Preface

For this second edition we again follow the general philosophy of the series by concentrating on those aspects of neonatal care which are of immediate clinical relevance to the anaesthetist, whether in the operating theatre or in the intensive care unit. We include essential new information on drugs and techniques and incorporate the new and greater understandings which are emerging from the increasing survival of babies with gestational ages as low as 26 weeks.

As before, the first chapter is devoted to perinatal physiology, because the differences between the anaesthetic needs for the newborn and the older child depend largely on differences in physiology. The chapter has been expanded to include new information in this field but we have continued to link anatomy, physiology, pharmacology and neonatal medicine with intensive care and anaesthetic practice. The title of this second edition has been extended to include perioperative care: this reflects our expansion of Chapters 2 and 4 to contain material which we hope will be of interest to non-anaesthetic medical colleagues, including surgeons and neonatologists, who are also involved in the care of small babies.

The contents of those chapters which deal with clinical matters are, as before, almost entirely based on our own experience at the Hospitals for Sick Children, Great Ormond Street, London, where more than 500 anaesthetics are administered annually to neonatal patients for all types of surgery. The clinical approach is based on concepts and techniques which have proved safe over many years of use. The references have again been limited to a brief list at the end of each chapter and contain only those we consider to be important or those which will provide an easy guide to further study of the subject.

Neonatal intensive care for medical problems has traditionally been the province of neonatal paediatricians and this volume does not attempt to cover all aspects of this subject which include, for example, detailed care of the very preterm baby and infant feeding. We have, however, mentioned those aspects of perioperative care which we believe are essential to the safe practice of neonatal anaesthesia. Because of the increasing survival of babies of low gestational age, the application of the term 'neonatal' has broadened and much of the information in this volume is now relevant to many babies beyond the first month of extrauterine life.

1986

D.J.H.
E.S.

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D.J.H.
E.S.

Contents

Perinatal physiology

Introduction and definitions

Prior to birth the fetus lives in a protected environment and, although most organs are capable of function even weeks before full term, it is not until after delivery that the functions of the placenta are at once replaced by the lungs, kidneys and gastrointestinal tract. After birth, itself a great physiological stress, the baby faces a harsh environment. The delivery may have been traumatic, and drugs and anaesthesia given to the mother may still be affecting the baby. After birth, organs and physiological systems develop at different rates; for example, the liver reaches maturity long before the kidneys or the central nervous system. The development of the neuromuscular junction is related to the length of extrauterine life rather than to gestational age. During the early days of life, adaptations occur in all systems, sometimes even with a transitional stage, to fit the baby eventually for adult life. The degree of maturity at birth and the rate at which these adaptations occur depend largely on the gestational or postconceptual age—the age at birth expressed in weeks after conception.

The neonatal period is generally regarded as the first 28 days of extrauterine life. By the end of this period most physiological systems have matured reasonably well in healthy infants born at term, but those of low postconceptual age may take considerably longer to mature. No magical change occurs on the 28th day, and many of the problems discussed in this book have relevance in older infants. The differences between the baby and the adult, however, are clearly greatest in the newborn neonate, especially if birth occurs before term.

Preterm infants can themselves be classified according to their weight as well as their gestational age (Fig. 1.1). Significant physiological differences occur, particularly with regard to metabolism, between preterm infants who are small for gestational age (SGA), appropriate size for gestational age (AGA) or large for gestational age (LGA). Both SGA and LGA babies have a higher mortality rate than AGA babies at all gestational ages, and an accurate assessment of postconceptual age is therefore essential when assessing the risks of anaesthesia. In the absence of a reliable menstrual history from the mother, postconceptual age can be approximated by careful examination of the baby (see p. 57), but accurate assessment may require estimation of the lecithin/sphingomyelin ratio of the amniotic fluid. This is discussed in more detail on p. 3.

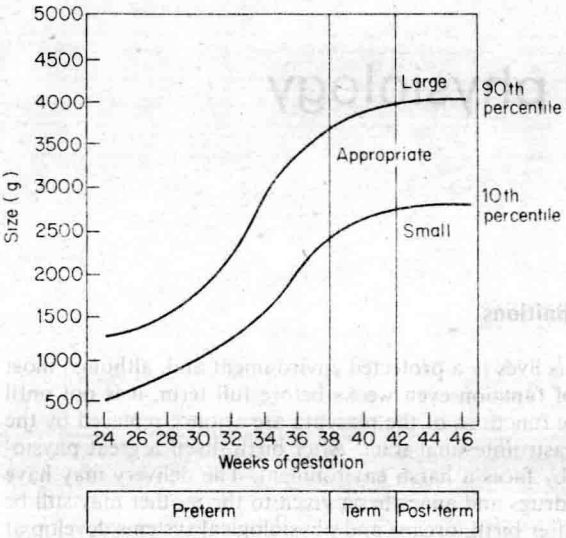

Fig. 1.1 Percentile chart of weight in relation to gestational age. (Reproduced, with permission, from Lubchenco, 1976)

Respiration

The lungs during fetal life

Before birth all gas exchange and acid–base balance is performed by the placenta, but the development of the lungs must prepare them to be able to take over full respiratory function by weeks 24–28 of gestation. The bronchial tree is fully developed by week 16, as are the preacinar blood vessels, whose development follows that of the airways. Respiration is not possible at this stage, however, because the airways are blind-ending tubules completely lined by non-respiratory cuboidal epithelium. During the fourth to sixth months the respiratory portion of the lung becomes delineated as blood vessels grow beneath this cuboidal epithelium, thinning it, whilst new branches, all with thin-walled epithelium, also develop. By week 28 the preacinar pattern of airways, arteries and veins is complete, the blood/gas barrier is thin and capillary vessels are present within the alveolar wall. Muscularization of the intra-acinar arteries does not however, keep pace with the appearance of new vessels.

Specialized type II pneumocytes of the alveolar epithelial lining become discernible by electron microscopy during the sixth month of gestation; these contain the osmophilic inclusion bodies widely thought to be the site of production of surfactam. This lipoprotein complex lowers surface tension in the fluid lining of the alveoli once a fluid/air interface has developed.

Without surfactant, the lungs would be unable to retain gas within them and would be unstable because the pressure within them required to prevent collapse due to surface tension is inversely proportional to their radius (Laplace formula). As areas of lung collapse, the collapsing forces increase and thus a state of unstable equilibrium exists. Although surfactant can be detected in lung extracts from human fetuses from week 23 onwards, the quantity which can be detected increases greatly towards term and this is one of the main reasons why the older fetus has a greater chance of surviving in air than those delivered very prematurely. Surfactant can be detected in fetal tracheal fluid by week 28 and clearly the potential for normal extrauterine life exists by this stage of development.

Recent work shows that it is possible to make accurate assessments of fetal maturity from measurements of biochemical substances in the amniotic fluid. The concentration of sphingomyelin in the amniotic fluid remains fairly constant throughout pregnancy whilst surfactant production is accompanied by the appearance of lecithin. A lecithin/sphingomyelin (L/S) ratio of more than 2.0 is normally present by weeks 35–36, and is 98 per cent accurate in predicting that an infant will not develop idiopathic respiratory distress syndrome of the newborn (RDS). The 2 per cent of infants with L/S ratios of 2.0 or more who do develop RDS usually have a history of asphyxia *in utero*, are born to diabetic mothers or have rhesus

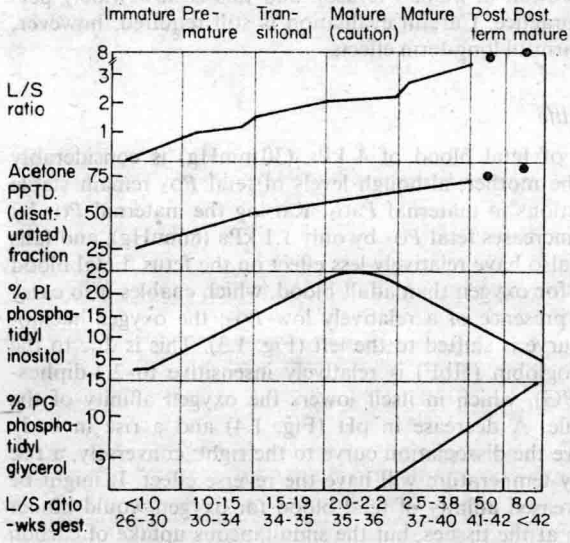

Fig. 1.2 Lecithin/sphingomyelin ratio and amniotic fluid phospholipids in relation to gestational age and lung maturity. (Reproduced, with permission, from Kulovich, Hallman and Gluck, 1979)

incompatibility and hydrops fetalis. Low L/S ratios (< 1.5) are less reliable predictors of lung development, as are intermediate values, and measurements of the acid phospholipids phosphatidyl inositol (PI) and phosphatidyl glycerol (PG) have been found to be more accurate. PI levels in amniotic fluid reach their peak by weeks 35–36, whilst PG appears by week 35 and peaks at birth (Fig. 1.2). The presence of PG indicates a definite degree of lung maturity and is not affected by diabetes or asphyxia.

During the last 3 months of gestation there is further differentiation of the respiratory region of the lung, with additional respiratory bronchioles developing whose terminal saccules are capable of acting as gas-exchanging areas. New alveoli continue to grow, however, until 8 years of age, and their size increases until adult life.

During fetal life the lungs are filled with fluid, and although the respiratory muscles contract vigorously from time to time from an early stage of development, they cannot move much fluid in and out because of the large frictional forces involved. Ultrasound studies in humans have clearly demonstrated that these breathing movements are a normal feature of fetal life, and they may well be essential for normal lung development. This view is supported by the fact that infants with spinal muscular atrophy which begins *in utero* have small lungs whilst those whose disease begins after birth do not.

A chance observation in fetal lambs (Liggins and Howie, 1972) showed that steroids infused into lambs born prematurely caused unexpected survival. It has since been confirmed that steroids injected into the mother accelerate lung maturation in human fetuses, and this is now widely performed in obstetric practice. Careful evaluation is still required, however, with respect to any harmful long-term effects.

Gas transport in fetal life

The oxygen tension of fetal blood of 4 kPa (30 mmHg) is considerably lower than that of the mother, although levels of fetal Po_2 remain stable even with wide variations in maternal Pao_2. Raising the maternal Po_2 by 20 kPa (150 mmHg) increases fetal Po_2 by only 1.1 kPa (8mmHg), and falls in maternal Po_2 will also have relatively less effect on the fetus. Fetal blood has a greater affinity for oxygen than adult blood, which enables it to carry more oxygen in the presence of a relatively low Po_2; the oxygen/haemoglobin dissociation curve is shifted to the left (Fig. 1.3). This is due to the fact that fetal haemoglobin (HbF) is relatively insensitive to 2,3-diphosphoglycerate (2,3-DPG), which in itself lowers the oxygen affinity of the haemoglobin molecule. A decrease in pH (Fig. 1.4) and a rise in body temperature will move the dissociation curve to the right; conversely, a rise in pH or fall in body temperature will have the reverse effect. It might be thought that the increased affinity of fetal blood for oxygen would hinder the release of oxygen at the tissues, but the simultaneous uptake of carbon dioxide shifts the dissociation curve to the right. Because the tissue oxygen tension is so low—about 2 kPa (15 mmHg)—and because the dissociation curve is so steep, adequate oxygen delivery to the tissues is ensured.

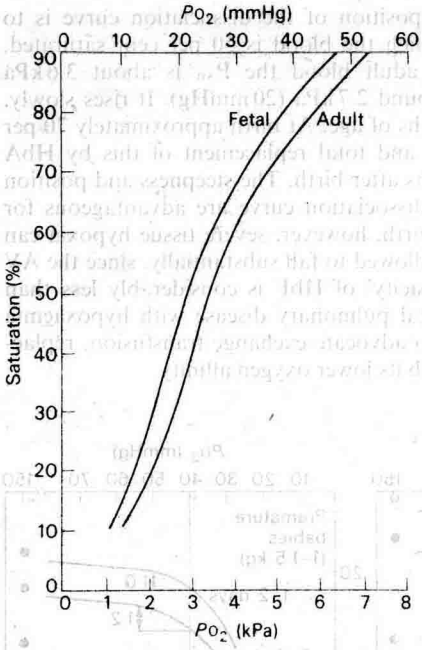

Fig. 1.3 Oxygen dissociation curves for fetal and adult blood. (Reproduced, with permission, from Darling *et al.*, 1941)

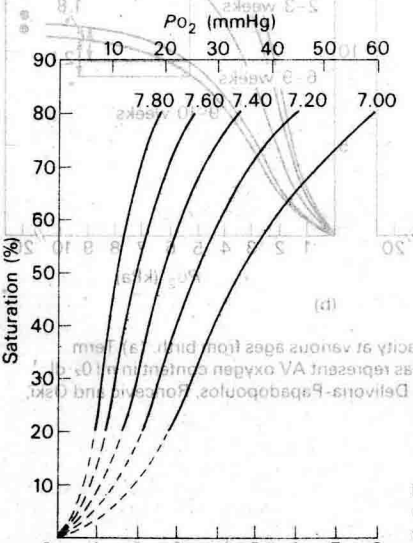

Fig. 1.4 Oxygen/haemoglobin dissociation curves for fetal blood at various pH levels. (Reproduced, with permission, from Hellegers and Schrueffer, 1961)

One method of expressing the position of the dissociation curve is to measure the oxygen tension at which the blood is 50 per cent saturated. This is known as the P_{50}. For adult blood the P_{50} is about 3.6 kPa (27 mmHg) whilst at birth it is around 2.7 kPa (20 mmHg). It rises slowly, reaching the adult value by 6 months of age. At birth approximately 70 per cent of the haemoglobin is HbF, and total replacement of this by HbA does not occur until about 3 months after birth. The steepness and position of the fetal oxygen haemoglobin dissociation curve are advantageous for normal fetal gas exchange. After birth, however, severe tissue hypoxia can occur if arterial oxygen tension is allowed to fall substantially, since the AV oxygen content or 'unloading capacity' of HbF is considerably less than that of HbA (Fig. 1.5). In neonatal pulmonary disease with hypoxaemia this factor has led some workers to advocate exchange transfusion, replacing fetal blood with adult blood with its lower oxygen affinity.

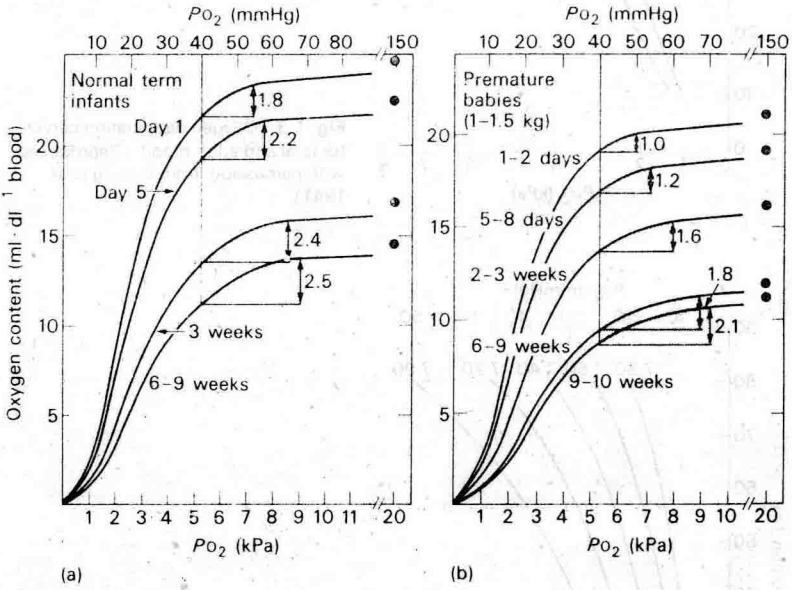

Fig. 1.5 The blood oxygen-releasing capacity at various ages from birth. (a) Term infants. (b) Preterm infants. The shaded areas represent AV oxygen content in ml $O_2 \cdot dl^{-1}$ blood. (Reproduced, with permission, from Delivoria-Papadopoulos, Roncevic and Oski, 1971)

Adaptation to extrauterine life

During vaginal delivery the baby's thorax is squeezed as it passes through the birth canal and up to 35 ml of fluid drains out of the mouth. As the

thoracic cage re-expands at birth, this volume of fluid is replaced by the entry of an equivalent volume of air into the trachea and main air passages. At birth the type II pneumocytes rapidly discharge their surface active phospholipids into the alveolar space, and are then seen to be vacuolated rather than containing dense inclusion bodies.

Many factors stimulate the newborn infant to take its first breath, including non-specific stimuli such as sound, touch, temperature and the effect of gravity, but one of the main factors appears to be a sudden resetting of the chemoreceptors. The sudden increase in sensory activity arising at the moment of birth activates the reticular system and causes a resetting of the respiratory centres, so that levels of oxygen and carbon dioxide tension which previously did not stimulate respiration now do so. The arterial oxygen tension falls during the birth process from its fetal level of about 4 kPa (30 mmHg); levels as low as 2 kPa (15 mmHg) have been reported. Increased glycogen stores protect the newborn infant to some extent from hypoxic tissue damage; CO_2 tension rises from about 6.7 kPa (50 mmHg) with a consequent fall in pH from its fetal level of 7.2. The reduction in blood flow through the umbilical vessels is also an important factor in initiating the onset of respiration, possibly by causing a sudden change in blood flow through the carotid bodies. The chemoreceptors are certainly not essential since, in experimental animals, respiration will start

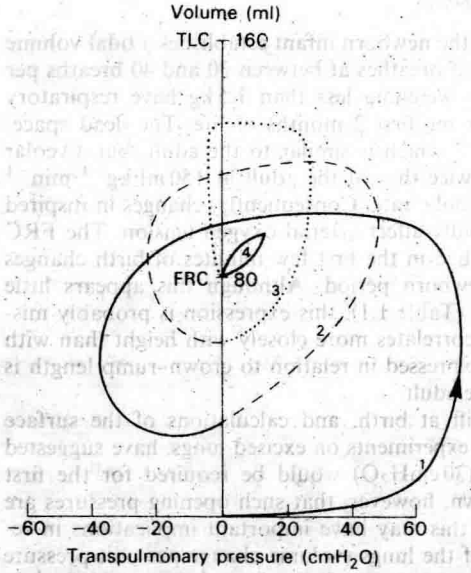

Fig. 1.6 The first four breaths. Each successive breath requires less pressure and adds increasing volume to the lungs. (Based on data from Karlberg and Koch, 1962)

if they are denervated. Chemoreceptor responses become sensitive to small changes in arterial blood gas tensions early in postnatal life.

After the onset of the first breath, which may require inspiratory pressures of 70 cmH_2O or more, a functional residual capacity (FRC) of 30–35 $ml \cdot kg^{-1}$ is rapidly established (Fig. 1.6). Remaining lung fluid is removed by the pulmonary lymphatics and lung capillaries which open up with lung expansion. A normal FRC is usually established within 60 minutes of birth. The rapid rise in arterial oxygen tension which follows the onset of respiration leads to a dramatic fall in pulmonary vascular resistance and an uptake of up to 100 ml of blood into the pulmonary circulation. The fall in pulmonary vascular resistance with increased pulmonary blood flow, together with a reduction in inferior vena caval return due to clamping of the umbilical cord, cause left atrial pressure to exceed right atrial pressure with closure of the foramen ovale. As the arterial oxygen tension rises, the smooth muscle in the ductus arteriosus constricts and closure is usually physiologically complete within 10–15 hours. These cardiac and pulmonary changes are obviously interrelated; ventilation improves both pulmonary perfusion and surfactant release, which in turn help further improve ventilation. Surfactant synthesis is dependent upon satisfactory oxygenation and acid–base state. The chain of events in newborns who fail to breathe immediately after birth is described in Chapter 6.

Respiratory function in the newborn

Over the first few hours of life the newborn infant establishes a tidal volume of approximately 6 $ml \cdot kg^{-1}$ and breathes at between 30 and 40 breaths per minute. Many healthy infants weighing less than 1.5 kg have respiratory rates of 50–60 per minute for the first 2 months of life. The dead space/tidal volume ratio is about 0.3, which is similar to the adult, but alveolar ventilation is approximately twice that of the adult at 150 $ml \cdot kg^{-1} \cdot min^{-1}$ due to the high neonatal metabolic rate. Consequently, changes in inspired oxygen concentration will rapidly affect arterial oxygen tension. The FRC of around 30 $ml \cdot kg^{-1}$ established in the first few minutes of birth changes very little throughout the newborn period. Although this appears little different from the adult value (Table 1.1), this expression is probably misleading because lung volume correlates more closely with height than with weight. FRC in the neonate expressed in relation to crown–rump length is significantly smaller than in the adult.

The lungs are relatively stiff at birth, and calculations of the surface forces involved, together with experiments on excised lungs, have suggested that a force of some 3 kPa (30 cmH_2O) would be required for the first breath. Recent work has shown, however, that such opening pressures are not required in practice, and this may have important implications in resuscitation. The compliance of the lungs (volume change per unit pressure change) increases over the first few hours from about 1.5 $ml \cdot cmH_2O^{-1}$ to about 6 $ml \cdot cmH_2O^{-1}$ (Fig. 1.7). By the end of the first week of life, however, the specific compliance (compliance/lung volume) is similar in value