

## Challenges in Perinatal Medicine

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One of the significant milestones in the perinatal care in Singapore is the birth of the Perinatal Society of Singapore in March 1989. This signaled the beginning of increased collaboration between the obstetricians and neonatologists in the management of high-risk pregnancies through multidisciplinary birth defect clinics and high-risk perinatal consultation services and this active partnership has grown over the years. Several advances have been made in the field of perinatal medicine during the last 15 years and they include antenatal diagnostic techniques and therapy, use of Doppler ultrasonography to assess fetal well being, antenatal steroid therapy, improved assisted ventilatory techniques, surfactant replacement therapy, inhaled nitric oxide therapy and enhanced parenteral/enteral nutrition. The above have contributed to significant reduction in perinatal mortality in Singapore.

This issue of the *Annals, Academy of Medicine, Singapore* offers a collection of articles contributed by experienced obstetricians and neonatologists. The short-term and long-term morbidity are high in the extremes of gestational age as well as birth weight. The focus of perinatal care in the 21st century has shifted from reducing perinatal mortality and morbidity to improving the long-term outcome of survivors. Numerous epidemiological studies give ample evidence for the fetal and infant origins of adult chronic diseases. Low birth weight or thinness at birth is associated with an increased risk of hypertension, central obesity, dyslipidaemia, insulin resistance, Type 2 diabetes, stroke and coronary artery disease in adult life.<sup>1,2</sup> 'Lifestyle' risk factors are probably addictive to the influence of early life. The associations are thought to be consequences of 'programming' whereby a stimulus or insult at a critical sensitive period of early life permanently alters the structure, physiology and metabolism of the adult offspring.<sup>3</sup> In this context, close monitoring of the growth and well being of the fetus is essential for early diagnosis and management of a pregnancy complicated by intrauterine growth restriction. The factors which influence fetal growth have been reviewed by Mongelli<sup>4</sup> in this issue. Few areas in medicine have evolved as rapidly during the past two decades as that of antenatal diagnosis. Increasing knowledge of fetal physiology has paved the way for effective fetal interventions and therapy. Tan and Yeo<sup>5</sup> have reviewed the recent advances in prenatal diagnosis and fetal therapy. With the combination of ultrasound and minimally invasive procedures, several disorders such as fetofetal transfusion syndrome, fetal hydrothorax, fetal anaemia and thrombocytopenia and fetal arrhythmias can be more effectively managed in-utero than in the past. Chorioamnionitis is a well-known risk factor for preterm delivery. Recent studies have shown that fetal inflammatory response syndrome that occurs in chorioamnionitis is characterised by elevated cytokine levels in the amniotic fluid and fetal blood.<sup>6</sup> This is postulated to cause accelerated but abnormal maturation of the fetal lung, leading to decreased incidence of respiratory distress syndrome (RDS), but increased incidence of chronic lung disease (CLD).<sup>7</sup> It has also been linked with increased risk of white matter lesions in the brain and cerebral palsy among survivors.<sup>8</sup> The paper by Fung et al<sup>9</sup> examines the relation between chorioamnionitis and RDS, CLD, cerebral lesions and neurodevelopmental outcome in a cohort of extremely premature infants. Also in this issue, there are two papers on obstetric cholestasis and changing trends in indications for caesarean sections respectively.

The article by Ho<sup>10</sup> provides valuable information on the history of neonatology in Singapore and also predicts future practice in neonatal care. This is followed by a review article on mass newborn screening, wherein Joseph<sup>11</sup> gives an overview on the existing screening programmes in Singapore and also provides projections for the future. Antenatal corticosteroid therapy prior to preterm delivery is the first proven antenatal pharmacological intervention that improved neonatal morbidity and mortality associated with preterm delivery. A single course of antenatal corticosteroids is safe and highly effective in reducing RDS, intraventricular haemorrhage, necrotising enterocolitis and also neurodevelopmental sequelae including cerebral palsy. However, there is less evidence to support the practice of multiple courses of corticosteroids, which may be associated with reduction in birth weight as well as lung weight and may cause neurologic impairment. Besides this, long-term follow-up studies of very preterm infants have raised concerns about the increasing use of postnatal dexamethasone in the neonatal intensive care units (NICUs) because of the growing evidence that

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dexamethasone may increase the risk of neurodevelopmental disability including cerebral palsy in survivors. Some of the above concerns are reviewed in depth by Rajadurai and Tan<sup>12</sup> in their paper.

Exogenous surfactant therapy has been a significant advance in the management of preterm infants with RDS and has become standard of care in most NICUs. It is one of the most extensively studied new therapies in neonatology. Over recent years, its use has been extended to non-RDS lung disorders, such as meconium aspiration syndrome, pulmonary haemorrhage, neonatal pneumonia and congenital diaphragmatic hernia. Suresh and Soll<sup>13</sup> have reviewed extensively the published evidence on exogenous surfactant therapy in newborn infants in this issue.

Rapid advances in neonatal intensive care have dramatically improved the survival of very-low-birth-weight (VLBW) infants. However, concerns have been expressed regarding the quality of long-term outcome among the survivors. Therefore, a specialised long-term follow-up programme should be an essential component of tertiary care perinatal centres and should preferably be coordinated by the NICU from which these high-risk infants graduate. This would enable systematic documentation of their growth and nutrition status and neurological, developmental, visual, hearing and behavioural problems during infancy, childhood and adolescence.<sup>14</sup> Two papers in this issue have been devoted to long-term follow-up and outcome of VLBW infants. Agarwal and Lim<sup>15</sup> have given an overview of the long-term follow-up and outcome of extremely-low-birth-weight (ELBW) infants, whereas Daniel et al<sup>16</sup> have reported on the 8-year outcome of VLBW infants from an institution-based study. The next step should be further collaboration between the perinatal-neonatal centres in the public and private sectors in Singapore, standardisation of the perinatal and follow-up audit programmes and generate population-based outcome data which would be of great help in evaluating the efficacy of perinatal-neonatal care. Networking with other perinatal centres in the region is also essential in order to monitor practice, facilitate clinical research and deliver the optimal evidence-based perinatal care.

With improved obstetric and neonatal care and technological advances, many marginally viable fetal infants (birth weight <500 g) and infants born at the threshold of viability (22 to 25 weeks) are surviving in increasing numbers. However, a major concern has been the high rate of severe handicap in those extremely tiny infants who survive. Thus, technological advances in neonatal intensive care have created ethical dilemmas in perinatal medicine. There are no easy answers for the question “How small is too small?.” In his paper, Ho<sup>17</sup> outlines the treatment dilemmas and ethical issues of perinatal care at the threshold of viability. The article also offers the clinician both cutting edge information on this complex issue and highly practical advice, transferable to the delivery room or NICU.

Indeed, we have much more to learn about the long-term consequences of events and interventions that take place during the perinatal period. I am sure this issue should provide useful and updated information for clinicians involved in the care of mothers and infants. I do hope it makes enjoyable reading to all our Fellows and doctors as well.

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